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THE CONTRACTILE AND ELECTRICAL PROPERTIES OF NORMAL AND MODIFIED HUMAN MOTOR UNITS

by

© HUNTLEY SANDY MILNER-BROWN

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES AND RESEARCH

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FACULTY OF GRADUATE STUDIES AND RESEARCH

The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies and Research, for acceptance, a thesis entitled "The Contractile and Electrical Properties of Normal and Modified Human Motor Units" submitted by H.S. Milner-Brown in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Physiology.

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ABSTRACT

1. The electrical activity of single motor units has been recorded from the first dorsal interosseus muscle of normal human subjects and patients with various neuromuscular disorders, during voluntary, isometric contractions, together with the force generated by the muscle. By averaging the force correlated with the impulses from a single motor unit, the contraction time, half-relaxation time and twitch tension generated by that motor unit could be measured. Under the experimental conditions the trains of impulses from different motor units in most subjects were generated quite independently. The frequency response for the contractions of a single motor units was well fitted by that for a linear, second-order system with nearly critical damping.

2. The first direct evidence that human motor units are recruited during increasing voluntary contraction in an orderly fashion according to the size of the contraction they produce, has been obtained. The relative importance of recruitment and increased firing rate, as mechanisms for increasing the force of voluntary contraction, was determined. Only at low levels of force is recruitment the major mechanism while increased firing rate becomes the more important mechanism at intermediate force levels and contributes the large majority of force if the entire physiological range is considered.

3. Two years after surgical repair of a unilateral complete severance of the ulnar nerve, the twitch tensions increased to normal size.

However, the normal orderly pattern of recruiting motor units of increasing size during increasing voluntary contractions was irretrievably lost. In patients with pressure or entrapment neuropathies and motor neuron disease, the orderly pattern of recruitment was not disrupted. Among patients with unilateral pressure or entrapment ulnar neuropathies, there was a tendency for the twitch tensions of single motor units to be smaller while the surface EMG amplitudes were generally larger in the affected hands. Very large EMG amplitudes but twitch tensions of normal size were observed among the motor neuron disease (amyotrophic lateral sclerosis) patients, indicating that in general motor units enlarged by sprouting are less efficient contractile units than units of normal physiological size.

4. Studies on synchronization were made on normal and neuropathic human motor units using the rectified and unrectified surface EMGs recorded from the first dorsal interosseus muscle of the hand, together with the EMG of single units recorded with a needle electrode. Of the thirty normals recorded from, only about 20% showed significant synchronization. The individuals showing synchronization were nearly all involved in occupations or sports which required near-maximal, brief activation of these muscles. To test whether this was responsible for the synchronization, an additional six weightlifters were studied. All showed significant synchronization. Among the patients with unilateral ulnar neuropathies who showed significant synchronization in their normal hands, there was a general decrease in or absence of synchronization in the

affected hands. Reflex experiments suggest that the cause of the synchronization is due to strong descending supraspinal pathways rather than to spinal reflex mechanisms.

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CHAPTER I

INTRODUCTION

The electrical activity of single motor units can be recorded so easily during normal voluntary contractions that these recordings are used routinely in the diagnosis of diseases affecting nerves and muscles (Lenman & Ritchie, 1970). However, only recently have attempts been made to record the contractile tension generated by single motor units in man (Buchthal & Schmalbruch, 1970; Sica & McComas, 1971). The methods used to measure tension involve the more difficult task of stimulating single motoneurons in whole nerves or branches of nerves after they divide close to the motor end-plates. With these methods fast and slow twitch motor units have been identified in human muscles, but whether different fiber types are used differently during normal voluntary contractions remains unclear.

In 1971 Doctors R.B. Stein and R. Yemm developed a method in which impulses recorded from a single motor unit are used to trigger a signal averager, which sums the forces recorded from the whole muscle as a function of time before and after these impulses. If the impulses from other motor units occur at random times relative to the single motor unit being studied, averaging will extract the tension changes produced by the single unit from the overall tension fluctuations in the muscle. This method, together with other general experimental techniques, have been utilized in an extensive study of the contractile and electrical properties of normal and neurologically abnormal human motor units.

1.1 Recruitment of motor units

A large number of parameters have been found to vary systematically with motoneuronal size, and this has become known as the *size principle* (Henneman, 1968). For example, the larger the cell body of a motoneuron, the higher is the conduction velocity of its axon (Kernell, 1966; Burke, 1968), and the stronger is the muscular contraction which is produced when it is stimulated (McPhedran, Wuerker & Henneman, 1965; Wuerker, McPhedran & Henneman, 1965; Burke, 1967). Larger motoneurons are also recruited at higher thresholds during reflex (Granit *et al.*, 1957) or intracellular, electrical stimulation (Kernell, 1966). The after-potentials of larger motoneurons are shorter (Eccles, Eccles & Lundberg, 1958) and the initial rate of firing is higher (Kernell, 1965). Larger motoneurons increase their rate of firing more rapidly with increasing stimulation (Kernell, 1966) and attain higher firing rates (Granit *et al.*, 1957; Kernell, 1965). Higher firing rates are necessary to produce fused contractions, because the twitches generated by larger motoneurons are briefer in time course and so the fusion frequencies are higher (McPhedran *et al.*, 1965; Wuerker *et al.*, 1965). Many other physiological and histochemical differences between fast and slow twitch motor units have been described (Burke *et al.*, 1971; Close, 1972).

Fast and slow twitch units have recently been demonstrated by stimulating single motoneurons in man (Buchthal & Schmalbruch, 1970; Sica & McComas, 1971). There is also some indirect evidence for the orderly recruitment of increasingly large motor units during human voluntary contractions (Olson, Carpenter & Henneman, 1968), based on the size of the action potentials recorded by needle electrodes in the

muscle. However, variations in the order of recruitment have also been found (Basmajian, 1963; Grimby & Hannerz, 1968, 1970).

1.2 Mechanisms involved in the gradation of voluntary contraction of muscle

Over the past forty years, there have been contradictory opinions on the role of the two mechanisms involved in the gradation of contraction. The force of a voluntary contraction can be increased either by (i) increasing the number of active motor units (RECRUITMENT), or (ii) increasing the rate of discharge of the motor units already active (FREQUENCY CODING or RATE CODING). Adrian and Bronk (1929) and later Smith (1934), Lindsley (1935), Gilson and Mills (1941), Seyffarth (1941) and Norris and Gasteiger (1955) observed that during strong contraction of limb muscles, the number of active motor units increased, while the discharge frequency increased up to 40-50/sec. This suggests that an increase in muscular contraction is due to an increase in the frequency of motoneuron discharge as well as to recruitment.

However, Bigland and Lippold (1954), in a study of motor units of hand muscles (adductor pollicis, abductor digiti minimi brevis), found a wide range of contraction strength within which frequency remained practically unchanged. Stating that the behaviour of individual motor units is not uniform, the authors nevertheless concluded that the gradation of contraction is brought about mainly by motor unit recruitment except in very weak and strong contractions. Bracchi *et al.* (1966) put forward an extreme view that motor unit discharge frequency of each muscle is stabilized and relatively low (about 20/sec in the muscles of

the arms and about 10/sec in those of the legs). They believed motor unit recruitment is the means by which contraction strength is increased.

More recently, Clamann (1970), in his studies on single motor units in human brachial biceps, concluded that his work "quantifies and expands on the common observation that, at low tension levels, frequency change is the chief means of grading tension, while at higher tension levels, recruitment is the predominant mechanism". Person and Kudina (1972), working on m. rectus femoris, concluded that "recruitment is undoubtedly the main reserve of contraction strength increase - however, the mechanism of frequency change is unsurpassed as far as precision and smoothness are concerned".

Using methods which will be described in detail in Chapter III, the twitch tensions were determined for a substantial fraction of the motor units in the first dorsal interosseus muscles of three subjects. This was done by averaging the steady discharge of single motor units at just above the threshold force level required to recruit these units. By following the discharge of some of the same units during controlled changes in voluntary contractions at suprathreshold levels, it was possible to determine quantitatively for the first time, the relative importance of recruitment and rate coding as mechanisms for increasing the force of voluntary contraction.

1.3 Ulnar neuropathies and motor neuron disease

The ulnar nerve is a continuation of the median cord of the brachial plexus, and contains fibers derived from C.8 and T.1 roots. In the upper arm, it passes between the biceps and triceps muscles in close

relation to the brachial artery and median nerve, and it passes through a groove behind the medial epicondyle of the humerus to reach the forearm. In the forearm, it supplies the flexor carpi ulnaris and the median half of flexor digitorum profundus. After entering the hand it divides into a superficial and deep branch. The superficial branch supplies the skin over the hypothenar eminence, and the palmar surface of the fifth finger, and the medial aspect of the ring finger. The deep branch has no sensory supply, and near its origin gives off branches to supply the hypothenar muscles. After curving laterally around the hook of the hamate it supplies the INTEROSSEI, and the third and fourth lumbricals, and the adductor pollicis (Fig. 1).

Following injury to the ulnar nerve, there are a number of well recognized histological and electrophysiological changes. If the nerve is completely severed, some re-innervation of the intrinsic muscles of the hand may occur without surgical intervention, particularly if the lesion is fairly distal along the course of the nerve. However, in most cases the nerve is explored surgically and the cut ends are rejoined by various suturing techniques. The regeneration of a peripheral nerve after repair results in the formation of an excess number of regenerating fibers formed by branching (Ramon y Cajal, 1928; Edds, 1953). These excess fibers may fail to make peripheral connections: motor branches that fail to re-innervate muscle fibers will atrophy and eventually disappear, whereas those that make peripheral connections will increase in size (Weiss & Edds, 1946; Sanders & Young, 1946; Aitken, Sharma & Young, 1947). In addition, some motor fibers become connected with muscle fibers they did not formerly innervate (Esslen, 1960) and

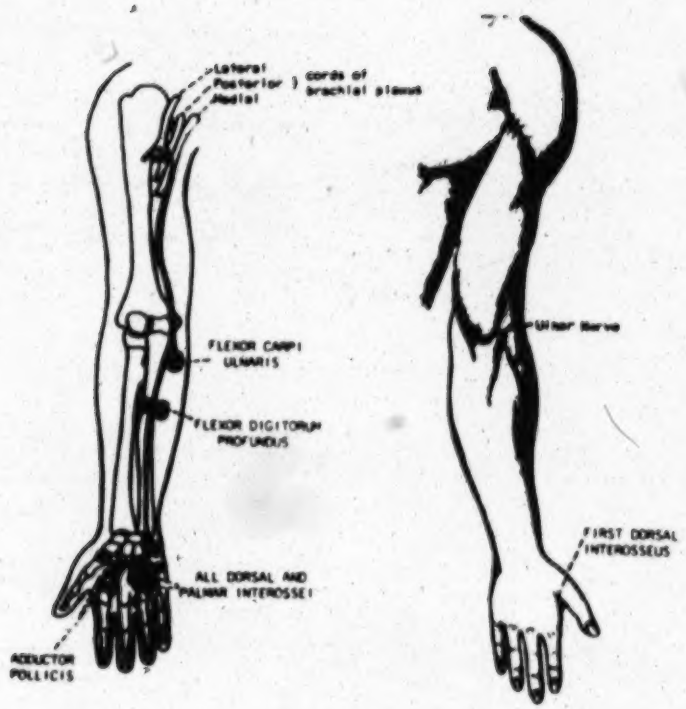

Fig. 1. Route of the ulnar nerve and some of the muscles innervated

hence give rise to new motor units that are functionally as well as morphologically different from the motor units prior to injury.

The ulnar nerve may be damaged as a result of localized pressure or entrapment at various sites along its course. The nerve is most vulnerable at the elbow, where it travels in a shallow groove behind the medial epicondyle. Here it may be damaged due to external pressure (either a single episode such as occurs during a period of unconsciousness or multiple episodes of pressure such as in the office worker who leans on his elbow). The nerve may also become entrapped and compressed in fibrous tissue in the ulnar groove, or it may be damaged as a result of a congenital or acquired deformity at the elbow, in which case repeated flexion and extension of the joint traumatizes the nerve (the so-called tardy ulnar palsy). Anterior transposition is frequently performed, but completely normal function is seldom regained (Seddon, 1972). The prognosis after surgery depends largely on the degree of nerve involvement, and Payan (1970) contends that the operation is being performed more often than necessary.

MOTOR NEURON DISEASE is a condition in which there is a progressive weakness and wasting of affected muscles, which is associated with degeneration of motor neurons in the brain and spinal cord. The two principal clinical varieties are referred to as amyotrophic lateral sclerosis and progressive muscular atrophy. In the latter variety, the process appears to be confined to the motor nerve cells, whereas in the former there is also degeneration of the corticospinal tracts giving rise to a combination of upper and lower motor neuron signs. Clinically, the onset is frequently associated with the appearance of wasting of the

small muscles of the hands, and widespread fasciculation may be an early feature. In some instances, weakness may start in the lower limb muscles or in the bulbar muscles, which are affected in the later stages of the disease.

Previous electrophysiological studies of motor neuron disease have indicated the following changes in motor unit properties (Erminio, Buchthal & Rosenfalck, 1959; Buchthal & Olsen, 1970): (i) increased amplitude of the individual motor unit action potential; (ii) increased amplitude of the interference pattern during strong voluntary effort; (iii) 30% or more increase in the mean duration of the motor unit action potential; and (iv) 80% or more increase in the territorial area of the motor unit. Very little, however, is known concerning the twitch tensions and other mechanical properties of these altered motor units.

A detailed electrophysiological study has been made of (A) five patients with a previous complete unilateral severance of the ulnar nerve; (B) fourteen patients with unilateral and four bilateral pressure or entrapment neuropathies affecting the ulnar nerve; and (C) eight patients with motoneuron disease (amyotrophic lateral sclerosis). These three groups are interesting in that there is a loss of physical continuity of all motor fibers in Group A, while in Groups B and C motor fibers are differentially affected. There is then a possibility that relatively normal motoneurons can sprout new collaterals and innervate more muscle fibers to compensate for the loss of other motoneurons (Coërs and Woolf, 1959). In Groups B and C there may be different effects due to the site of the lesion which will most severely affect

nerve conduction (Group B) or the properties of the cell body (Group C).

I.4 Synchronization of motor units

Motor units may function both independently of one another or discharge in groups. This form of grouping is SYNCHRONIZATION, i.e., coincidence in time (which exceeds random coincidence) of the discharges of two or more motor units. The occurrence of synchronization has been described as arising in exceptional cases in normal muscle (Hoefer & Putman, 1939; Buchthal & Clemmesen, 1941). Buchthal and Madsen (1950) found 20% synchronization in a large population of normal subjects, using the biceps muscle. In addition they found a variation in synchronization between different muscles as well as changes in synchronization among patients with various neurological disorders. Person and Kudina (1968), using cross-correlation analysis of two EMGs led off from the same muscle (biceps brachi), revealed synchronization of motoneuron discharges during fatigue and intense contraction, and also as an after effect of poliomyelitis.

Quantitative studies on synchronization have been made on normal subjects, on patients with ulnar neuropathies and motor neuron disease, and on weightlifters. The initial study on seven normal subjects will be presented in Chapters IV and V, while subsequent studies on patients and weightlifters will be considered in Chapters VI and VII. In the literature, the cause of synchronization has been discussed only on a somewhat hypothetical basis. Independent reflex experiments were therefore performed on weightlifters and controls, with the purpose of investigating any other changes that might take

place in the central nervous system as a result of weightlifting, which would shed some light on the main cause of synchronization of motor units.

This thesis can thus be divided into two main parts. The first part is on the contractile properties of normal human motor units, the focus being on the mechanisms involved in the gradation of voluntary contraction. The second part deals with the contractile and electrical properties of human motor units in neuropathies and motor neuron disease. The main study on synchronization of motor units will be incorporated in the second part.

This thesis includes most of the work the candidate has been directly involved in since the fall of 1971. Much of this material has been published or is in press jointly with Doctors R.B. Stein, R. Yemm and R.G. Lee (Milner-Brown, Stein & Yemm, 1973a, b, c; Milner-Brown, Stein & Lee, 1974a, b; Stein & Milner-Brown, 1973, 1974). The Results and Discussion presented in Chapters IV and V follow the published versions closely, which were largely prepared for publication by Doctor R.B. Stein. The Results and Discussion presented in Chapters VI and VII contain more unpublished material. Where material is included which is in press, it was largely prepared for publication by the thesis candidate.

CHAPTER II

GENERAL BACKGROUND AND THEORETICAL REVIEW

This chapter reviews some of the important phenomena, theoretical ideas and assumptions which were utilized in this study. These include the electromyogram, linear systems and statistical theory.

II.1 The motor unit

Within a muscle, the axon from a single motor nerve cell arborizes into many terminal branches. Each branch is attached to an individual muscle fiber. The branching of the axon permits a single neuron to stimulate a group of muscle fibers. For example, an electrical impulse travelling along a single axon will induce the contraction of approximately 200 fibers in the first dorsal interosseus muscle of the hand (Feinstein *et al.*, 1955). The functional unit of the neuromuscular system thus differs from the structural units of the nerve and muscle systems which are, respectively, the neuron and the muscle fiber. The functional unit of the neuromuscular system is the *motor unit; it consists of the anterior horn cell, its axon and all the muscle fibers innervated by that axon.*

II.2 The electromyogram

Muscular contraction is caused by depolarization of the muscle fibers. This depolarization causes a muscular action potential known as the electromyogram or EMG. The EMG can be picked up by needle electrodes inserted into the muscle or by surface electrodes placed over the muscle

concerned. The shape of the surface EMG is triphasic or diphasic, the first two phases coinciding with the phase of depolarization of the intracellular action potential; the second phase occurs near peak. The shape of the extracellular action potential (surface EMG) recorded with two electrodes in an unlimited conducting medium can be predicted by simple arguments based on the spread of action currents. Ahead of the depolarized region of the fiber current flows out of the fiber, i.e., the potential decreases radially and is therefore positive since it is zero far from the fiber. In the depolarized region conditions are opposite: current flows into the fiber, i.e., the potential decreases towards the fiber and is negative in this region. This explains the two main phases of the surface EMG. Finally, currents which leave the fiber in the region under repolarization give rise to a terminal positive deflection.

II.3 Second-order linear system approximation

If the tension in response to an impulse in a motor unit can be approximated by the impulse response of a critically damped second-order system, then tension would be given as a function of time $f(t)$ by (Milsum, 1966)

$$f(t) = at\, e^{-t/T} \qquad \text{II.1}$$

Time delays such as occur in excitation-contraction coupling have been ignored. The peak tension occurs when the slope of $f(t)$ against t is 0, i.e., when:

$$df(t)/dt = ae^{-t/T}\,(1 - t/T) = 0 \qquad \text{II.2}$$

Equ. II.2 will obviously hold when $t = T$, so the constant T simply represents the contraction time of the motor unit. The value of the peak tension P can then be obtained by setting $t = T$ in equ. II.1:

$$P = f(T) = aT/e \qquad \text{II.3}$$

From equs. II.1 and II.3, half-relaxation will occur when:

$$f(t) = aT/2e = ate^{-t/T}$$

or after rearrangement:

$$2e(t/T)e^{-t/T} = 1$$

This occurs when $t = 2.68T$. Thus, the half-relaxation time should be nearly 1.7 times as long as the contraction time (this will be discussed in Chapter V).

The area under the curve of equ. II.1 (tension-time integral) gives the total number of g-sec contributed by the twitch to the overall force in the muscle.

$$\begin{aligned}\int_0^\infty f(t)dt &= aT^2e^{-t/T}\,(1 + t/T)\Big|_0^\infty \\ &= aT^2 \\ &= PTe \text{ (using equ. II.3)}\end{aligned} \qquad \text{II.4}$$

Equ. II.4 indicates that for this linear approximation, each impulse will produce a contribution of PTe g-sec, where P is the twitch tension, T is the contraction time and e = 2.72 is the base of the natural logarithms. This prediction will be tested in Chapter IV.

II.4 Frequency response functions

If a constant parameter linear system is physically realizable and stable, then the dynamic characteristics of the system can be described by a frequency response function $G(f)$. When $x(t)$ is the time dependent input to a system and $y(t)$ is the output, the frequency response function $G(f)$ of the system may be obtained from:

$$G(f) = \frac{S_{xy}(f)}{S_{xx}(f)} \qquad \text{II.5}$$

and the coherence function $\gamma^2(f)$ from:

$$\gamma^2(f) = \frac{|S_{xy}(f)|^2}{S_{xx}(f) \cdot S_{yy}(f)} \qquad \text{II.6}$$

where

$S_{xx}(f)$ = power spectral density of $x(t)$

$S_{yy}(f)$ = power spectral density of $y(t)$

$S_{xy}(f)$ = cross-spectral density

The coherence function is a measure of the degree of linearity of the input-output relationship. The frequency response function is generally a complex valued quantity and may be thought of in terms of a magnitude and associated phase angle. $G(f)$ can thus be written as

$$G(f) = |G(f)|e^{-j\phi(f)} \qquad 11.7$$

The absolute value $|G(f)|$ is called the GAIN, and $\phi(f)$ the PHASE. In these terms, the frequency response function takes on a direct physical interpretation as follows. Assume a system is subjected to a sinusoidal input with a frequency f producing an output which will also be sinusoidal with the same frequency. The ratio of the output amplitude to the input amplitude is equal to the gain $|G(f)|$ of the system, and the phase shift between the output and input is equal to the phase $\phi(f)$ of the system. Now

$$\log |G(f)|e^{j\phi(f)} = \log |G(f)| + j\phi(f) \qquad 11.8$$

The log-log plots of gain and phase against frequency are called Bode plots. Fig. 2 gives the Bode plots for a critically damped basic second-order system. The frequency response for a single motor unit during a voluntary isometric contraction will be given in Chapter IV.

The AUTOCORRELATION FUNCTION for random data describes the general dependence of the values of the data at one time on the values at another time. The CROSS-CORRELATION function for two sets of random data describes the general dependence of the values of one set of data on the other. A roundabout method for computing autocorrelation and cross-correlation function estimates is to first compute by fast Fourier transform procedures the power spectral density functions, and then to compute the inverse Fourier transforms of these results. The double use of fast Fourier transform procedures to compute both the spectral density

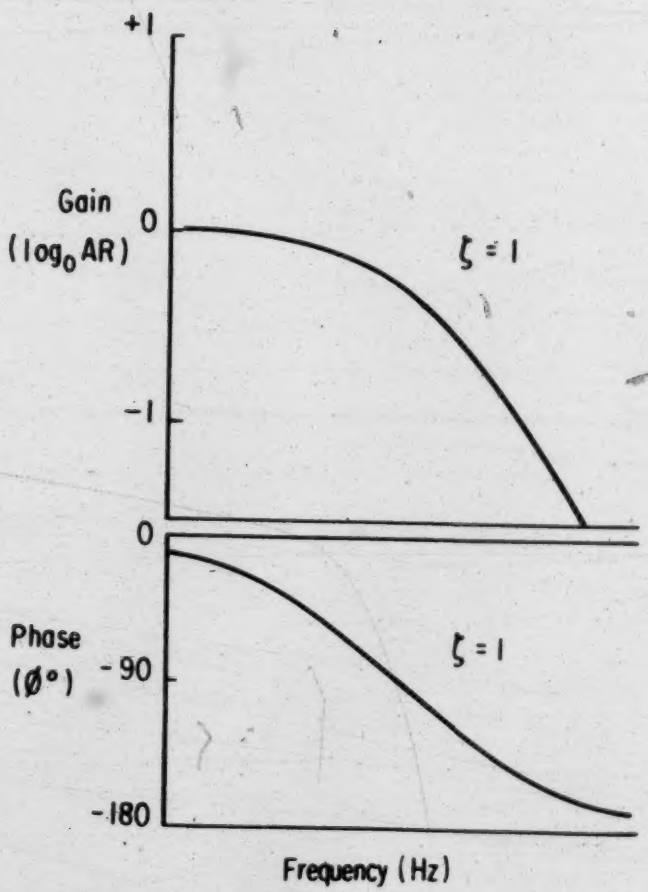

Fig. 2. Bode plots for a critically damped basic second-order system

functions and the correlation functions can make this total operation more efficient than direct computation of average products among the sample data values (Bendat & Pierson, 1971). The autocorrelation and cross-correlation histograms of motor unit impulses will be given in Chapter IV.

II.5 Statistical theory

This section deals with the relevant statistical methods used in this study.

The normal distribution: A variate that follows the frequency function

$$f(x) = \frac{1}{\sigma\sqrt{2\pi}} \exp^{-\frac{(x-\mu)^2}{2\sigma^2}} \qquad (-\infty < x < \infty) \quad \text{II.9}$$

is said to be normally distributed with mean value of μ and a variance of σ^2. The normal distribution is quite often a fairly good approximation to the distribution of random fluctuations in biological and physical phenomena.

Student's t-distribution: In sets of size $(n+1)$ from a normal distribution the ratio of the average to standard deviation $(t = \bar{x}/s)$ follows Student's t-distribution with n degrees of freedom. The probability density function for the t-distribution is

$$f(t) = \frac{\Gamma[(n+1)/2]}{\Gamma(n/2)} \cdot \frac{1}{\sqrt{n\pi}} \cdot \frac{1}{(1 + t^2/n)^{(n+1)/2}} \qquad (-\infty<t<\infty) \quad \text{II.10}$$

mean value of $t = 0$, variance of $t = \frac{n}{n-2}$ $(n>2)$.

The gamma function Γ is defined by

$$\Gamma(x) = \int_0^\infty u^{x-1} e^{-u}\, du$$
$$\Gamma(\tfrac{1}{2}) = \int_0^\infty u^{-\frac{1}{2}} e^{-u}\, du = \sqrt{\pi} \qquad 11.11$$
$$\Gamma(1) = \int_0^\infty e^{-u}\, du = 1$$

There are Tables of the values of t exceeded in absolute value with probability α, i.e., t_0 for which

$$\int_{-t_0}^{t_0} f(t)\, dt = 1 - \alpha \qquad 11.12$$

Correlation coefficient: Let x and y be two variables for each of which the deviations from the average have a normal distribution. Then for a set of corresponding pairs $x_1, y_1;\ x_2, y_2;\ \ldots;\ x_n, y_n$ the correlation coefficient of the sample is

$$r = \frac{\Sigma(x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\Sigma(x_i - \bar{x})^2\ \Sigma(y_i - \bar{y})^2}} \qquad 11.13$$

where $\bar{x} = \frac{1}{n}\Sigma x_i$, $\bar{y} = \frac{1}{n}\Sigma y_i$.

For $r = 0$ there is no correlation. For $r = 1$ there is strict proportionality $y = Cx$.

Test of whether a correlation coefficient is different from zero: If r is the observed correlation coefficient found in the linear regression case, assumed to be an estimate of ρ of a bivariate normal

distribution, then in order to test the null hypothesis that $\rho = 0$ against the alternative hypothesis that $\rho \neq 0$ compute the statistic

$$t = \frac{r\sqrt{n-2}}{\sqrt{1-r^2}}$$

When the null hypothesis is true t follows Student's t-distribution for $(n-2)$ degrees of freedom. Reject the null hypothesis if the observed value of t is greater than the value of Student's t-distribution exceeded in absolute value with probability α. For example in Chapter VI, Fig. 28 gives the twitch tension against threshold force two years after complete severance of the ulnar nerve. The correlation coefficient of 0.44 substituted into the above statistic gives $(n=11)$

$$t = \frac{0.44}{\sqrt{1 - (0.44)^2)}} \quad 9$$

$$= 1.3$$

From Statistics Tables of Student's t-distribution $\rho = 1.3$ at 20%, i.e., $r = 0.44$ is not significant even at 20% level of significance.

To test whether the mean of a normal distribution is greater than a specified value: Observed values, $\bar{x}$ and s based on n measurements considered as a set of values from a normal distribution with mean μ, and standard deviation σ.

Null hypothesis: $\mu = \mu_0$

Alternate hypothesis: $\mu > \mu_0$

Test statistic: $t = \frac{\bar{x}-\mu_0}{s\sqrt{n}}$

t follows Student's t-distribution for n-1 degrees of freedom if null hypothesis is true.

Rejection criterion: Null hypothesis is rejected if the observed value of t is greater than the value of t for n-1 degrees of freedom, exceeded with probability α.

Kolmogorov-Smirnov λ *test*: The significance of a difference between the distributions of the same parameters in the normal and affected hands, to be discussed in Chapter VI, was calculated using the Kolmogorov-Smirnov λ test (Fisz, 1963). This section explains the method.

Let $Q_n(x)$ be the distribution function of the random variable $D_n\sqrt{n}$,

$$Q_n(x) = \begin{cases} P(D_n\sqrt{n} < \lambda) = P(D_n < \frac{\lambda}{\sqrt{n}}) & \text{for } \lambda > 0 \\ 0 & \text{for } \lambda \leq 0 \end{cases} \qquad 11.14$$

$$\lim_{n\to\infty} Q_n(x) = Q(x) = \begin{cases} \sum_{k=-\infty}^{n} (-1)^k \exp(-2k^2\lambda^2) & \text{for } \lambda > 0 \\ 0 & \text{for } \lambda \leq 0 \end{cases} \qquad 11.15$$

This is the Kolmogorov-Smirnov distribution.

Suppose $X_{11}, X_{12}, \ldots X_{1n1}, X_{21}, X_{22}, \ldots X_{2n2}$ are independent random variables with the same distribution function $f(x)$. Let $S_{1n1}(x)$

and $S_{2n2}(x)$ be the empirical distribution functions of the first and second group of random variables respectively. Thus, $S_{1n1}(x)$ and $S_{2n2}(x)$ are the empirical distribution functions of two independent simple samples drawn from the same population in which the characteristic x has the distribution function $f(x)$, and n_1, n_2 are the sizes of the samples respectively.

Let

$$D_{n_1n_2} = \max_{-\infty<x<\infty} [S_{1n1}(x) - S_{2n2}(x)] \qquad 11.16$$

$n = \frac{n_1n_2}{n_1+n_2}$ and $Q_{n1n2}(x)$ is the distribution function of the random variable $\sqrt{n}\, D_{n1n2}$

$$Q_{n_1n_2}(x) = \{P(D_{n_1n_2} < \lambda/\sqrt{n}) \qquad \text{for } \lambda > 0 \qquad 11.17$$

For an example of the application of the Kolmogorov-Smirnow λ test, we select two independent simple samples from a population in which the characteristic x has a continuous distribution function $n_1 = 70$, $n_2 = 100$, and the observed value of $D_{n1n2} = 0.18$. What is the probability that $D_{n_1n_2}$ is smaller than this value?

Solution: $n = \frac{n_1n_2}{n_1+n_2} = 41.2$, $\sqrt{n} = 6.42$

$$\lambda = D_{n_1n_2}\sqrt{n} = 0.18 \times 6.42 = 1.16$$

from Smirnov's limit theorem

$$P(D_{n_1n_2} < 0.18) = P(D_{n_1n_2} < \frac{1.16}{6.42}) = Q(1.16)$$

From Statistical Tables $Q(1.16) = 0.864$ or Probability that $D_{n_1n_2} > 0.18$ is

$1 - 0.864 = 0.136$

i.e. $P < 0.15$

CHAPTER III

METHODS

All the motor units studied were from the first dorsal interosseus muscle of the hand. This particular muscle was chosen for extensive study because it is the only one producing movement of the index finger away from the middle finger (there is no corresponding ventral interosseus muscle). Also, since we intended to correlate the tension generated with the discharge of single motor units, a fairly small muscle having a limited number of motor units was desirable.

III.1 EMG recording

One bipolar needle electrode (except during cross-correlation studies when two needle electrodes were used) was inserted into the muscle and positioned so that the discharge of single motor units could be distinguished at a moderate level of voluntary contraction. The electrodes consisted of two fine (75 µm) wires for differential recording fixed with epoxy in the barrel of a needle (25 gauge) which served as a ground connexion. The potentials picked up by the electrodes are usually very small in amplitude and consequently must be amplified to a level that can be conveniently handled by the other apparatus. The AMPLIFIER designed for this purpose should have the following characteristics: (1) high and uniform voltage gain for all frequencies within its stated range; (2) a frequency range of 20-10,000 Hz; (3) differential input; (4) high input impedance; and (5) high common-mode rejection.

Input impedance: is the ratio of the voltage applied to the input to the current drawn by the amplifier. In most applications, it is desirable to have the input impedance many times greater than the impedance of the electrode. This ensures that very little current is drawn from the source of the potential to be amplified, and there is minimal drop of voltage at the electrode. If the input impedance is lower than the electrode impedance, a condition known as "loading", a large current will flow from the source through the electrode and amplifier impedance, causing a comparatively large voltage loss across the electrode and a reduced voltage available for the amplifier. This condition results in distortion of the potential wave shape.

Differential input: A differential amplifier is characterized by its rejection of voltages which are identical (in both amplitude and time) at its two input terminals and the amplification of the voltage difference between the two input terminals. When an electrode is inserted into or placed on a muscle it will pick up action potentials; however, it may also pick up 60 Hz signals from power supplies or poor grounding or other sources. The latter potentials, if passed through an ordinary single-ended amplifier, would be amplified along with the muscle potentials. In this type of recording the quality of the amplifier output, especially if the action potentials are low amplitude, would be very poor. To improve the quality of the recording, a differential amplifier is used for the first stage of amplification. The differential amplifier simply amplifies the difference in voltage that exists at every instant between signals applied to the two inputs.

For example, two voltages identical in amplitude and phase that are applied to the differential amplifier will cause no output voltage. In-phase signals arising from power lines or from sources outside the electrode field which would normally interfere with the desired action potentials will be rejected by the amplifier. The ability of a differential amplifier to reject identical signals is called *common-mode rejection.*

Frequency response: defines how fast an instrument can respond without distortion to changes of voltage at its input. A factor of considerable importance in our quest for faithful reproduction of source potentials is the ability of the apparatus to follow reliably any changes in potential with time. If the apparatus cannot follow the fast changes, then both the amplitude and duration of the recorded signals will be inaccurate. The frequency response of electrodes and amplifier are similar to that illustrated in Fig. 3. In selecting the best frequency response for the EMG amplifier, two factors must be considered: (1) no distortion of any recorded potentials; and (2) noise voltages maintained as low as possible. If we choose a wide frequency range to ensure distortion-free recording, we may also allow noise, which is introduced via the electrode or amplifier wiring, to pass through the amplifier. Consequently, the frequency response is carefully chosen on the basis of the frequency content of the EMG potentials and the elimination of potentials of all other frequencies.

During each recording, the electrical activity was (1) amplified using a preamplifier with 10 MΩ input impedance and 90 dB common-mode

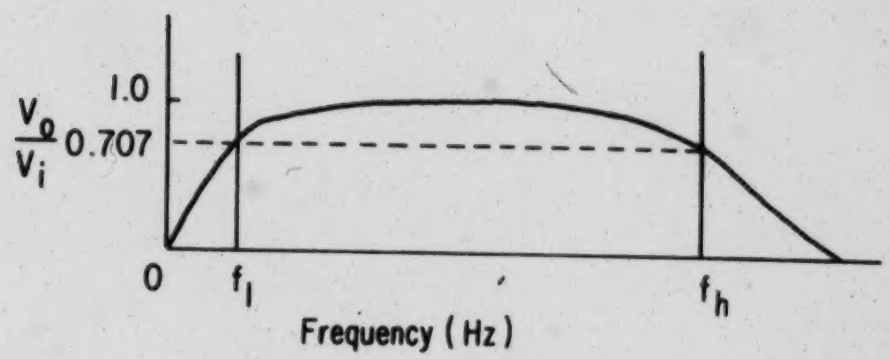

Fig. 3. A frequency response characteristic for an amplifier. f_H is high frequency cut-off, f_L is low frequency cut-off, V_o/V_i is ratio of voltage output to input.

rejection (Tektronix Type RM-122 Low-level Preamplifier); (2) filtered with a low-frequency cut-off between 80 and 100 Hz and a high-frequency cut-off of 1,000 or 10,000 Hz; (3) displayed on an oscilloscope; and (4) recorded on an FM tape recorder. Subjects were provided with both visual and auditory feedback of the electrical signals, as suggested by Basmajian (1963) and were asked to maintain the discharge of a single motor unit at a slow, fairly steady rate (e.g., 5-10 impulses/sec). Single units were identified in the usual way, by triggering the oscilloscope from the amplified electrical signal, and observing the occurrence of a repetitive waveform with (1) invariant amplitude and time course; and (2) no intervals shorter than several msec. Although some units could be made to discharge steadily at somewhat lower rates, this often proved difficult to maintain for the periods of recording used (3 min). The voluntary force level was then varied to change the firing rate or to recruit other motor units and the process was repeated. After recording all the motor units that could be distinguished at one electrode location, the position of the electrode was changed. Attempts were made in each session to record motor units which were recruited over a range of forces from very weak ones up to a Kg or more. Pulse height analyzers (Stein, 1968) were available to analyze smaller units which were recorded simultaneously with units producing larger electrical signals. In addition to a needle inserted into the muscle, silver disc surface electrodes (with a diameter of 9 mm) were often placed 3±0.5 cm apart on the skin on opposite sides of the needle and electrode paste was used for good electrical contact. The three electrodes were then in a line parallel to the long axis of the muscle.

Similar amplification, filtering and recording were used for the surface EMG. In later recordings (Chapter VI) a 5 msec electronic delay was introduced before recording the surface EMG so that its full time course could be observed when triggering from the needle EMG.

III.2 Tension recording

In the first part of this study (Chapters IV and V), subjects held a force transducer between their thumb and first finger, while resting their arm comfortably on a support. The force transducer was rigidly clamped to the support. In later studies, however (the results of which are given in Chapter VI), the force transducer was rigidly clamped to a metal rod fixed in the center of a table and the subjects rested their arms comfortably on the table. Brackets were mounted on the frame of the transducer for the thumb and on the lever attached to the strain gauges to accommodate the lateral portion of the first finger, approximately midway between the base of the finger and the proximal interphalangeal joint. The transducer was virtually isometric, allowing only 1 mm of movement, and was used with springs for recording forces up to about 2 Kg. The natural frequency of the transducer when loaded by the bracket was about 400 Hz. Where the records after averaging were noisy, the higher frequencies were sometimes filtered, taking care not to distort the recorded waveform. Low frequency fluctuations were commonly seen in the tension records, and these were reduced before recording by a high-pass filter with a time constant of 1 or 2.5 sec. This does not appreciably distort the time course of any

traces shown here which have, at most, a duration of 320 msec.

III.3 Correlation and averaging methods

The four-channel FM tape recorder was used to record (1) the unfiltered force at low gain; (2) the force at higher gain after filtering out low frequency fluctuations (see Tension recording); (3) motor unit activity from a needle electrode; and (4) the activity from either a second needle electrode or the surface EMG. The activity from motor units could be replayed through a predetection facility about 270 msec before the corresponding force records. The impulses from single motor units were used to:

1. trigger an averager. The averager would then sum the force records and/or the surface EMG from a number of sweeps (typically 512) to determine the magnitudes of the signals correlated in time with the impulses from a single motor unit, or trigger a general purpose laboratory computer (LAB-8, Digital Equipment Corp.) and 500 sweeps were generally averaged.
2. generate an *autocorrelation* histogram (Moore, Perkel & Segundo, 1966) using a computer program (French, 1970) which measured the numbers of impulses occurring at various time intervals after the occurrence of an impulse in a single motor unit. The numbers of impulses were divided by the number of sweeps and bin width to give the rate of discharge following an impulse which is referred to in various applications as an autocorrelation histogram, as a renewal density function or an intensity function (Stein, 1972). The numbers of impulses were also summed and divided by the number

of sweeps to give the cumulative mean number of impulses occurring in various intervals following an impulse.

3. generate a *cross-correlation* histogram for distinct trains of impulses recorded with two needle electrodes (Moore *et al.*, 1966). The numbers of impulses in one train which occur at various times before or after the occurrence of an impulse in the second train were measured and converted to a rate of discharge as for the autocorrelation histogram.

Rate limitation: It was often desirable for reasons explained under Results to average only those impulses which occurred at least a time T msec removed from other impulses. A block diagram of a simple circuit to select such impulses automatically is shown in Fig. 4.

III.4 Synchronization

The presence of synchronization was quantitatively evaluated using the rectified and unrectified surface EMG records. The surface EMG was passed through a full-wave rectifier, and then averaged as a function of time before or after the occurrence of impulses from a motor unit recorded by a needle electrode. The effect of this process is shown schematically in Fig. 5. The time of occurrence of impulses recorded by the needle electrode are indicated by a vertical line in Fig. 5A. Associated with these impulses will be some waveform on an unrectified average (indicated schematically by a triangular waveform in Fig. 5B). Impulses from other units which are not tightly synchronized (approximately to within the time T) will be "averaged out" because

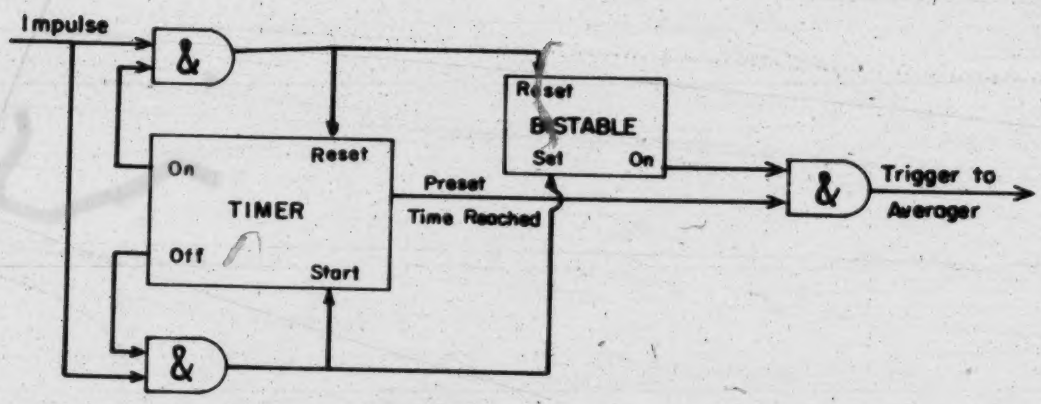

Fig. 4. Block diagram for the rate limiter. The circuit contains three gates which perform a logical AND function; e.g., a trigger pulse is sent to the averager only if a preset time T has been reached *and* the bistable is on. The timer switches off after reaching the time T and the bistable is only set if an impulse arrives when the timer if off; i.e., when no impulse has occurred for the time T beforehand. Thus an output is produced a time T after an impulse only if both the preceding and succeeding intervals are greater than T. This corresponds to choosing impulses occurring with a maintained rate less than $1/T$. Using the predetection facility of the tape recorder, the trigger pulses could actually start the sweeps 270 - T msec before the corresponding force or surface EMG records.

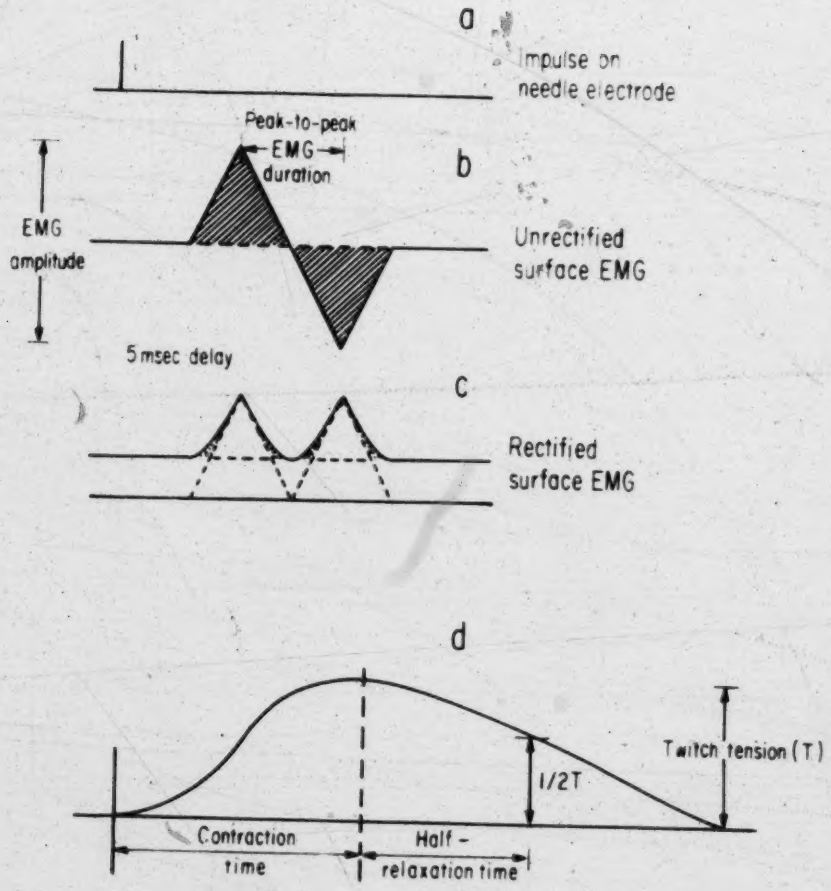
a
Impulse on
needle electrode
Peak-to-peak
EMG
duration
b
EMG
amplitude
Unrectified
surface EMG
5 msec delay
c
Rectified
surface EMG
d
Twitch tension (T)
1/2T
Contraction
time
Half -
relaxation time

Fig. 5. Schematic representation of the averaged twitch tension, with the parameters of the twitch which are routinely measured (d) and a test for synchronization of motor units using the unrectified and rectified surface EMGs (a)-(c). If a laboratory computer is triggered by impulses from a single unit (a) recorded by a needle electrode, a waveform (b) is obtained by directly averaging the surface EMG. When impulses in different motor units are generated independently (no synchronization), this average will simply represent the average voltage generated by the single unit which is recorded by the surface electrodes (the area indicated by diagonal lines in (b)). If averaging is done after rectification (c), there will be a net contribution to the average of (1) the waveform in (b) after rectification; (2) the ongoing activity of other units; and (3) a slight degree of summation between these two (dotted area). However, if the discharge of several units tends to be grouped (synchronization) a broader and larger increase in the rectified surface EMG will be observed than can be accounted for by (1) to (3) above.

there will be an equal probability that they will give a positive or a negative contribution on successive sweeps. (Because of the AC recording, the time average of these EMG waveforms must be zero.) It can be shown (Cox & Miller, 1966) that the probability density function $f(v)$ for the total voltage v contributed by other, uncorrelated units in individual traces will be Gaussian with a standard deviation σ, i.e.,

$$f(v) = (2\pi\sigma^2)^{-1/2} \; e^{-\frac{v^2}{2\sigma^2}} \; dv \qquad (1)$$

After rectification there will be a net contribution where

$$\bar{v} = 2(2\pi\sigma^2)^{-1/2} \int_0^\infty v \; e^{-\frac{v^2}{2\sigma^2}} \; dv = (2\sigma^2/\pi)^{1/2} \approx 0.8\sigma \qquad (2)$$

If we consider the average waveform at a time when the single unit always add an amplitude a, the net voltage $\bar{v}$ will be

$$\bar{v} = (2\pi\sigma^2)^{-1/2} \left[\int_{-a}^\infty (v+a) \; e^{-\frac{v^2}{2\sigma^2}} \; dv + \int_a^\infty (v-a) \; e^{-\frac{v^2}{2\sigma^2}} \; dv\right]$$

$$= (2\pi\sigma^2)^{-1/2} \left[2\int_a^\infty v \; e^{-\frac{v^2}{2\sigma^2}} \; dv + \int_{-a}^{+a} (v+a) \; e^{-\frac{v^2}{\sigma^2}} \; dv\right]$$

$$= (2\sigma^2/\pi)^{1/2} \left[e^{-u^2/2} + u \int_0^u e^{-u^2/2} \; du\right] \qquad (3)$$

where $u = v/\sigma$. In Fig. 5C, the interrupted lines show the contribution to the rectified average expected from rectification alone (equ. 2), and from the EMG measured in the unrectified average alone. The solid line above these is the summation predicted by equ. (3). Note that very

little summation occurs at the two extremes of amplitude. This can be shown mathematically from equ. (3) since for small values of u

$$\overline{v} \simeq 0.8\sigma \ (1 + 1/2u^2)$$

while for u greater than about 3, $\overline{v} \simeq \sigma$. The maximum summation (when $\sigma = 0.8$) is only 30%, and the increase in area due to summation (the shaded portion above the interrupted lines) can be computed for any waveform using equ. (3). With the waveform of Fig. 5B the summation is only 9%. The expected summation depends on the actual waveforms recorded and a summation of 20% was considered as a reasonable lower limit for synchronization activity. In general the synchronization ratios (given by the dotted area in Fig. 5C over the area indicated by the diagonal lines in Fig. 5B) obtained might have been underestimated, since the maximum delay available for the surface EMG was 5 msec. Synchronized activity recorded on the surface more than 5 msec before the impulses from a motor unit was therefore neglected.

III.5 Spectral analysis

In addition to these analyses in the time domain, computer programs were available to calculate as a function of frequency (1) the spectrum of the force record; (2) the spectrum of an impulse train; (3) the cross-spectrum between the force record and an impulse train; and (4) the best fitting linear frequency response function for the force related to the impulse train. This is obtained by dividing the cross-spectrum by the spectrum of the impulse train (Bendat & Piersol,

1966). For our purposes the shape of the impulses was not of interest. Therefore, the programs treat the trigger pulses as Dirac δ-functions filtered appropriately for the frequency band considered. These programs, including their assumptions and limitations for the analysis of neural data, have been described in detail elsewhere (French & Holden, 1971a, b, c).

"Threshold" force for recruitment: Subjects were asked to maintain the force at a level just adequate for activating a given motor unit to discharge steadily. The force necessary to do this was read from a calibrated solid state Digital Voltmeter (Triplett Model 8000) early in a recording period of about 2 min. Any changes later during the recording period were also noted, but not used in the data to be presented. Sometimes the threshold force declined, but more often, particularly with high threshold units, the threshold increased during the period of recording.

III.6 Tracking of triangular waveforms

In order to examine how the firing rate varied with force, subjects were asked to track triangular waveforms, while recordings were made from a bipolar needle electrode inserted into the first dorsal interosseus muscle of the hand. The waveforms were displayed on an oscilloscope after summing with a square wave which had a high repetition rate (1000 c/s), and an amplitude equal to 6% of the peak-to-peak extent of the waveform. The summation produced a visual display consisting mainly of two horizontal lines which moved up and down the oscilloscope

at a constant rate. The force generated by the subject against a stiff tension transducer (compliance = 0.5 mm/Kg) was displayed on the second beam of the oscilloscope. The subject was asked to press against the force transducer with the lateral edge of his first finger so as to keep the force within the limits set by the horizontal lines. Subjects learned this task readily, and were able to keep the force within the limits most of the time. The range of forces required to track the triangular waveforms varied from 400 g to 1,600 g. The base of the triangle was usually adjusted to a level about equal to the passive force of the hand resting against the transducer. The standard cycle time (the time for one repetition of the triangular waveform) was 10 sec, but this was varied in later experiments as described under Results (Chapter IV).

Signals from (1) a bipolar needle electrode; (2) surface EMG electrodes; (3) the force transducer; and (4) a waveform generator were recorded on four channels of an FM tape recorder as described earlier. In replaying the signals, each impulse from a single motor unit was used to reset a digital counter after shifting the value of the previous interval into a simple digital-to-analogue converter for display (Stein, 1968). Thus, the *duration of the last complete interval* could be plotted, together with the force generated, on two channels of a pen recorder. A smooth curve of interspike interval against time was drawn by eye, and the following measurements were made from the fitted curve (see Fig. 6):

1. the interspike interval and the force level at which the discharge began (note that by using the fitted curve, we smoothed the records

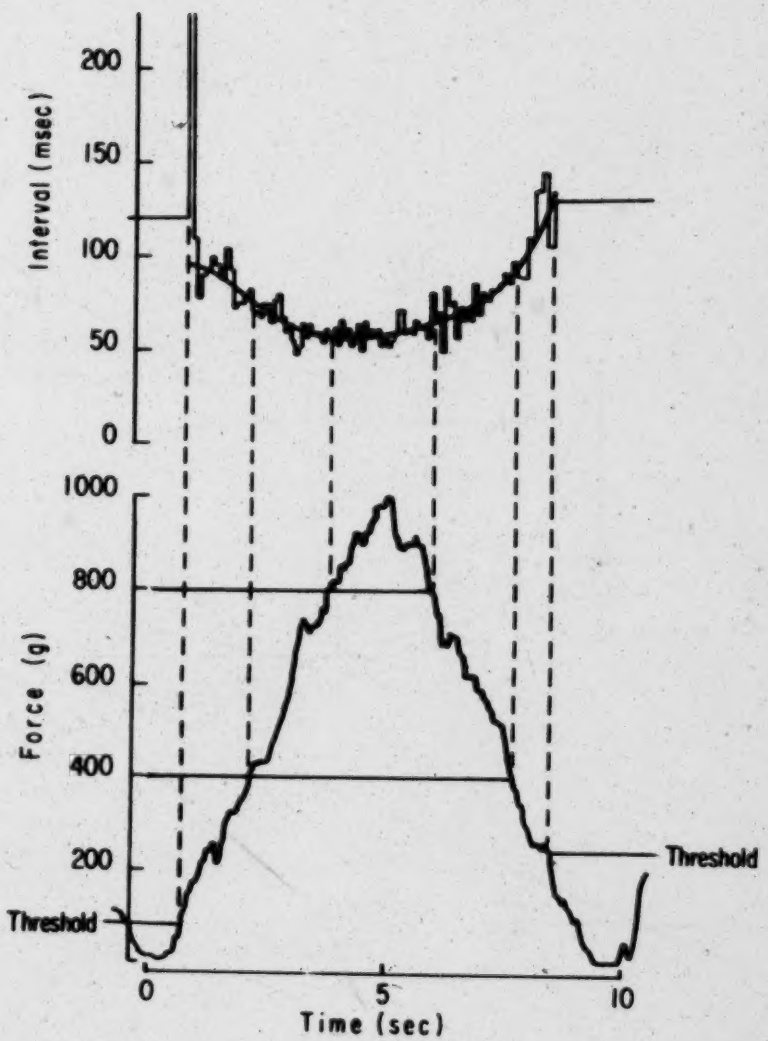
200
150
100
50
0
Interval (msec)
1000
800
600
400
200
Force (g)
Threshold
Threshold
0
5
10
Time (sec)

Fig. 6. Continuous record of interspike intervals from a single motor unit (upper tracing) and force (lower tracing) generated by the muscle in tracking a triangular waveform which required 1 Kg of effort. The interrupted lines indicate the measurements made, as indicated in the text, at threshold and at predetermined values of force (e.g., 400 and 800 g on the rising and falling phases of the force record. The value of interspike interval plotted on the pen recorder (to an accuracy of ±2.5 msec) is that of the preceding interval, so the last interval before the unit stopped firing is held, and a long interval (> 250 msec) is plotted as soon as the force surpasses threshold and the unit again begins to fire.

and took into account the first few intervals);

2. the intervals when the force passed various, predetermined levels on the rising and falling phase of the waveform; and
3. the interval and force level at which firing ceased on the declining phase of the triangular waveform. Typically about ten waveforms were averaged, and the inverse of the mean interval (mean rate of firing) was computed, together with the S.E. of the mean.

III.7 Reflex experiments

The abductor pollicis brevis muscle was used in these experiments because the reflex effects being studied were best illustrated in this muscle. A position on the wrist where the electrical stimulus produced maximum contraction of the muscle was first located. A stimulating electrode filled with conductive jelly was then fixed at this point. Stimulation pulses, 60-100 V (depending on the subject), duration 0.2 msec, were generated by a Grass S-8 stimulator at a rate of 0.5-1/sec. The electrical activity of the muscles was recorded with surface electrodes, and fed through a Tektronix 122 differential amplifier, with the gain set at 100 and the frequency bandwidth 8 Hz to 1 KHz. The potentials were displayed on the oscilloscope viewed by the subject, filtered and recorded on an FM tape recorder (Hewlett Packard), then rectified and 200 sweeps averaged on line on a general purpose laboratory computer (LAB-8, Digital Equipment Corp.). While recording the EMG from the muscle, evoked potentials are simultaneously recorded from the cervical region of the scalp over the hard area of the motor cortex (Cracco, 1972) using surface electrodes. The neck, ear and scalp

are first cleaned with alcohol. The electrode was attached to the scalp using colloidon, and filled with conductive jelly. The contralateral ear was used as reference electrode. The evoked potentials were fed through a Grass P-15 Preamplifier, with gain set at 1,000 and frequency bandwidth 3 Hz to 1 KHz. After passing through operational amplifiers the evoked potentials were displayed on an oscilloscope, recorded on an FM tape recorder and either the spinal or cortical potential averaged on line. Recordings were made under three different conditions. Initially the subject was asked to relax completely and the maximum M wave was elicited by median nerve stimulation. Then the subject was asked to maintain about 1 Kg force and finally an attempt was made to make volitional effect maximal at the moment when the stimulus was applied. The three conditions were repeated often with submaximal stimuli. From the data on dectapes and magnetic tapes, the following parameters were obtained for each subject: Maximum M, V_1, V_2, V_3 (see section VI.3 for explanation of notation) and the amplitudes and latencies of the spinal and cortical evoked potentials. The ratios $\frac{V_1}{M}$, $\frac{V_2}{M}$ and $\frac{V_3}{M}$ were then calculated for each subject. The maximum peaks of the spinal and cortical evoked potentials and the corresponding latencies were also noted.

Circuitry: Fig. 7 is a diagram of the electrical circuit used in most of the recording. 122_1 and 122_2 are differential preamplifiers (Tektronix Type RM-122 Low-level Preamplifiers), gain = 1,000. The gains on the operational amplifiers were set so that the inputs to the tape recorder and computer do not exceed 1 V. Operational amplifier O is a

low-pass filter, *P*, non-inverting unit gain operational amplifier, and *N* is a multiplier/divider. Fig. 8 is the circuit diagram used only for the reflex experiments.

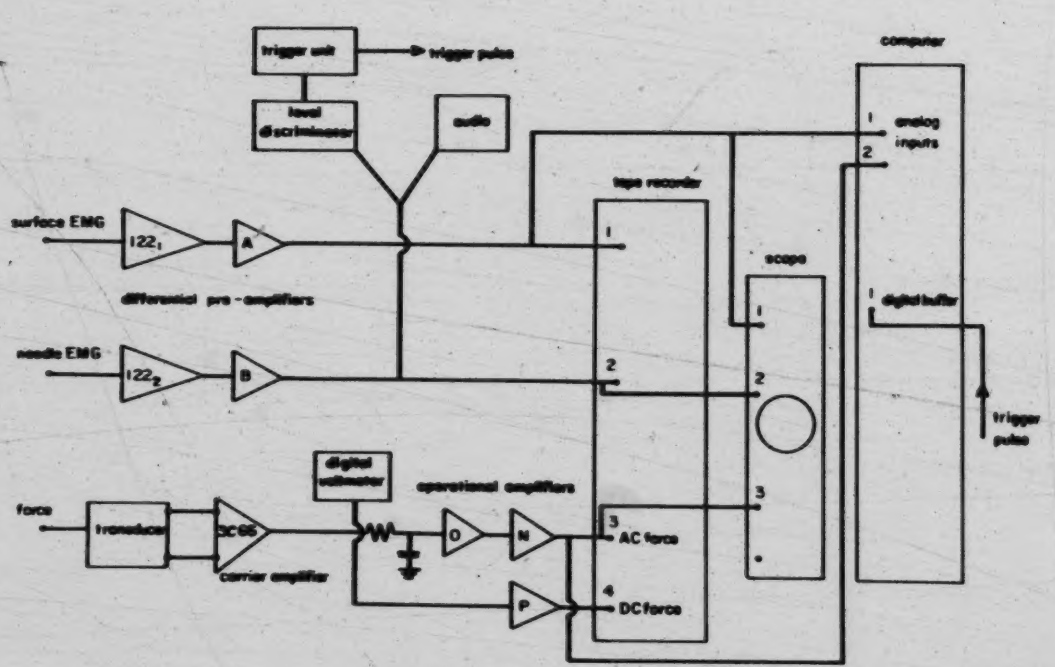

Fig. 7. Circuit diagram used for recording, the needle EMG, surface EMG, and force. Operational amplifier, *O*, is a low pass filter, *P* - non-inverting unit gain operational amplifier, and *N* is a multiplier/divider. The computer is a general purpose laboratory computer (LAB-8, Digital Equipment Corp.).

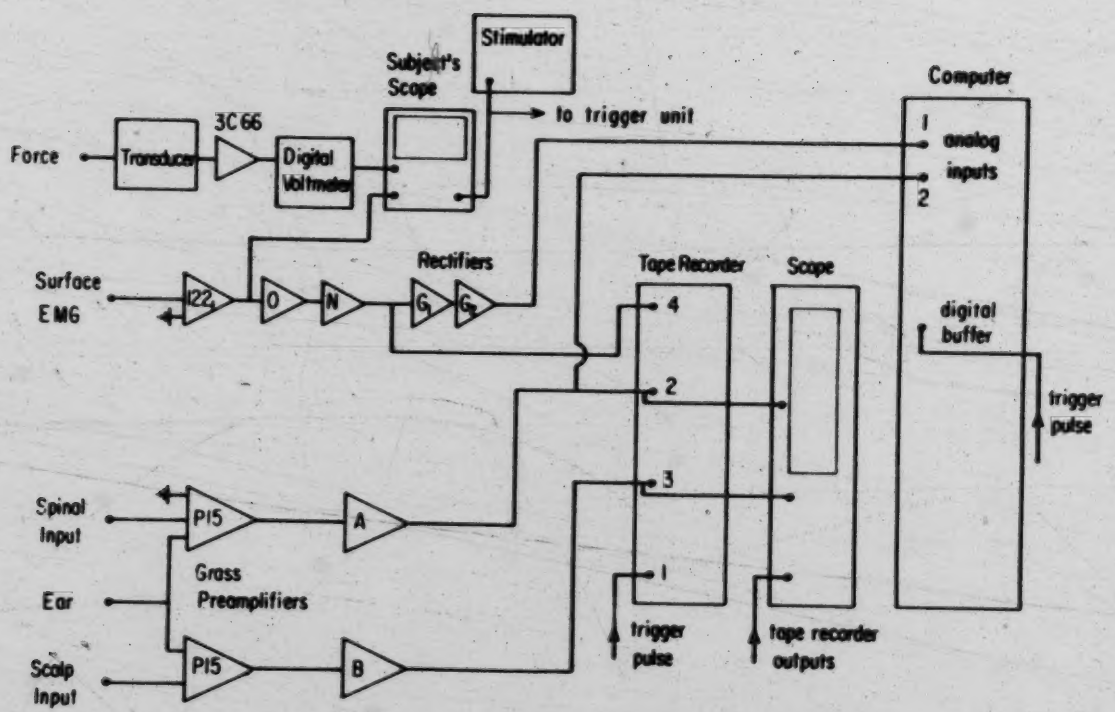

Fig. 8. Circuit diagram used in reflex experiments for recording EMG, and evoked spinal and cortical potentials. Details in text.

CHAPTER IV

RESULTS (I)

The results will be presented in two separate Chapters. The first set of results in this Chapter IV deals with normal human motor units and all the averaging was done using an averager (Biomac 1000). The results will be presented under the subheadings (1) The contractile properties of human motor units during voluntary isometric contractions; (2) Orderly recruitment of human motor units; and (3) Changes in firing rate of human motor units during linearly changing voluntary contractions. This will be followed by a related Discussion in Chapter V.

The second set of results on abnormal human motor units will be presented in Chapter VI.

IV.1 The contractile properties of human motor units during voluntary isometric contractions

Fig. 9 shows the results of averaging the force correlated with the impulses from single motor units. The predetection facility of the tape recorder was used together with a delay so that approximately 10 msec of the force record is seen before the occurrence of the impulses from the motor units. In Fig. 9A the force record begins to rise sharply after a latency of a couple of msec, and reaches a maximum of 0.7 g at a time 45 msec after the beginning of the impulses. The time interval for the force to decline from the peak to half its maximum value (half-relaxation time) is 25 msec. As seen in the lower part of

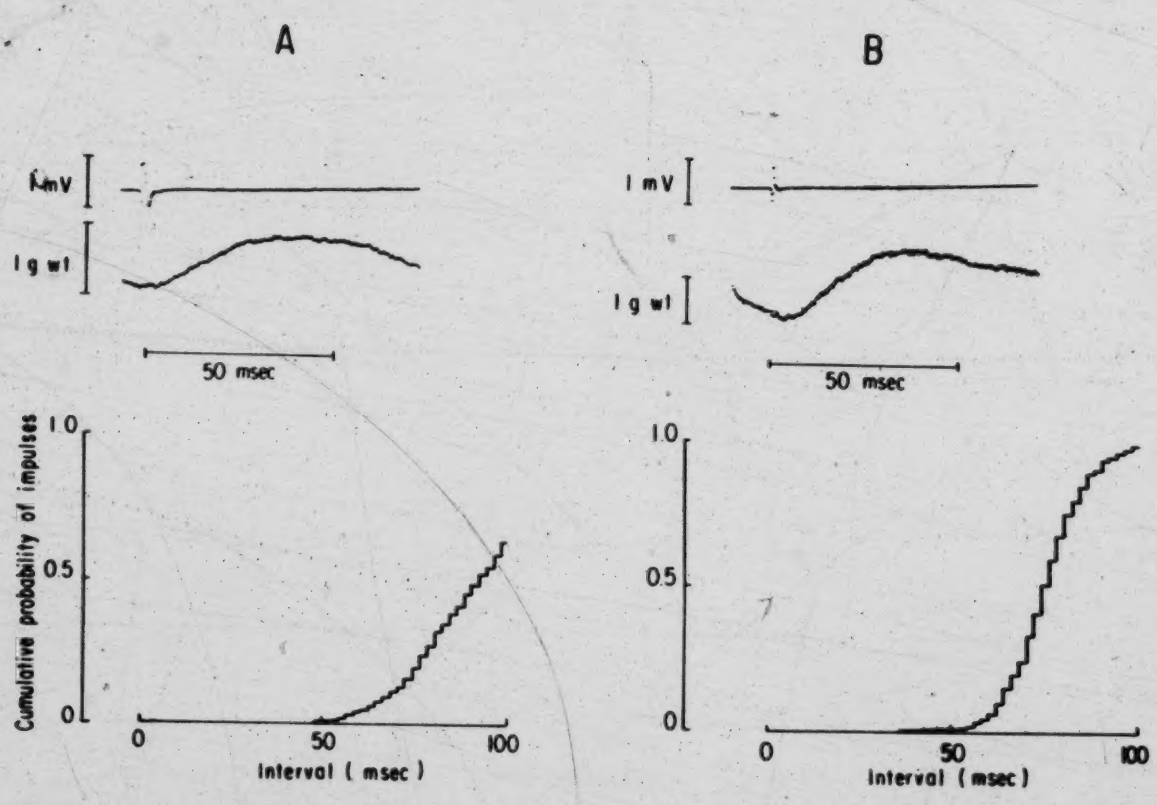

Fig. 9. Average responses correlated with the discharge of single motor units. Shown from top to bottom are the average waveform of impulses recorded by a bipolar needle electrode, the average force correlated with the occurrence of these impulses, and the cumulative probability of impulses occurring within the intervals indicated following the impulses at 0. The two parts A and B were recorded from different subjects and show units which were firing with different mean rates (10.5 and 13 impulses/sec).

this figure, subsequent impulses only occurred during this time on about 10% of the sweeps, so most of the force changes observed represent the largely unfused twitches produced by this motor unit. A small degree of fusion is indicated by the fact that the tension from preceding impulses had not decayed completely (note the slow decline of tension before the occurrence of the triggered impulses).

Sometimes the discharge could not be maintained at low rates and the average force had a more fused appearance (Fig. 9B). The tension from preceding impulses was still decaying quite markedly before the occurrence of the triggered impulses. Subsequent impulses occurred commonly after an interval of about 60 msec, so the falling phase of the tension record is slowed and does not reach the half-relaxation point. However, the somewhat higher force (1.5 g) and somewhat briefer contraction time (40 msec) are easily measured. In order to check that these values did not vary markedly with the rate of discharge from single motor units, the contraction time and maximum force were measured at two different rates in fourteen motor units (typically about 7 and 10 impulses/sec). The arithmetic mean ratio of the contraction times at the higher rate to that at the lower rate was 1.022±0.027 (mean ± S.E.) while the ratio of the tensions was 1.35±0.14 (mean ± S.E.). The geometric mean for the ratios of maximum tension was 1.26. These values are not significantly different from unity so that measurements of contraction time and twitch tension generated by the motor units do not appear to depend strongly on firing rate, despite some degree of fusion.

Rate limitation: Occasionally, the discharge rate was high enough that even the peak tension was unclear. In order to measure the twitch tensions and contraction times for such units, and to measure the half-relaxation times for units such as shown in Fig. 9B, it was desirable to select out those portions of the discharge where the motor unit was firing at a lower rate. A circuit is described in the Methods (Fig. 4) for selecting only those impulses where the preceding and succeeding impulses occurred at an interval greater than T msec. This effectively limits the analysis to those portions of the record where the rate of firing is being maintained at below (1,000/T) impulses/sec. This rate limiter was of considerable value in analyzing motor units from subjects who had no previous experience in controlling the discharge of single motor units, and for analyzing those motor units, even in experienced subjects, which could not be maintained for several minutes at a low rate.

The effect of selecting increasingly long minimum intervals is shown in Fig. 10B-D, using the same unit as in Fig. 9B. In Fig. 10B no limitation was used, and the trace is similar to Fig. 9B except that the duration of the sweep was twice as long. Generally a value of T could be selected (Fig. 10C) where (1) the tension fell well below the maximum value before the occurrence of later impulses; and (2) the tension preceding the triggered impulses was not significantly altered. In this way accurate values for the contraction time and twitch tension could always be obtained. The values of the half-relaxation time (30 msec in Fig. 10C) were more difficult to obtain (see also *Stimulation* below).

A further difficulty is illustrated by the bottom trace (Fig.

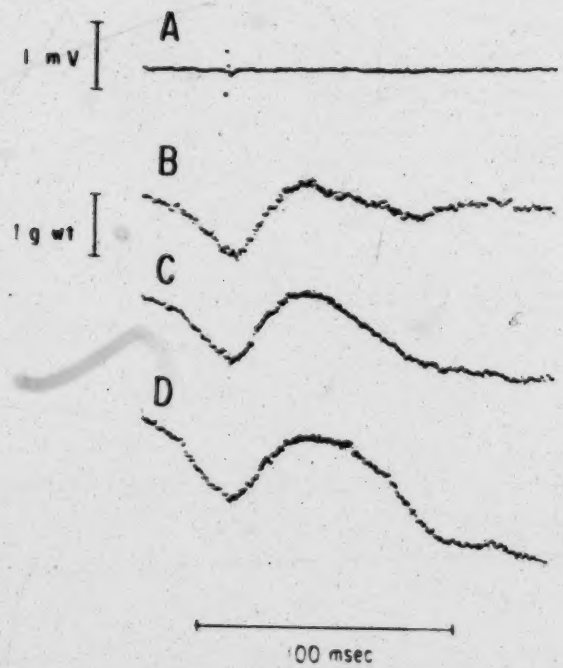

Fig. 10. Average forces correlated in time with the discharge of the single motor unit shown in A (same unit as in Fig. 9B). No limitation of rate was imposed in B. In C and D impulses which occurred with preceding and succeeding intervals shorter than 65 msec and 70 msec respectively have been excluded using the rate limiter (Fig. 5). Further explanation in text.

IOD) in which an increased negative slope is observed even *before* the triggered impulses occurred. This trace was obtained from the fraction of impulses where both the preceding and succeeding intervals were longer than 70 msec. Spontaneous slow fluctuations in force were generally seen and the longest intervals were apparently more common when the mean force level was slowly declining (see also Clamann, 1970). Because of these difficulties half-relaxation times could only be measured in a fraction of the units studied.

The observation of trends in the data with extreme rate limitation raises the general question of the effect other motor units have on the average values measured for a given motor unit. To demonstrate that these average values represent the contractile properties of single motor units, one must show that *the impulses from other motor units did not tend to occur grouped together in time with those from the single motor unit being studied (synchronization).* Therefore, we examined the degree of synchronization between motor units in this muscle under the conditions of our experiments in three ways by (1) stimulation experiments; (2) averaging the total activity recorded with the surface EMG which was correlated in time with the impulses from a single motor unit; and (3) measuring the cross-correlation between the firing times of two motor units recorded simultaneously by separate needle electrodes. These results will be examined in turn in the next three sections.

Stimulation: In several experiments the needle electrode was carefully positioned so as to record the largest possible signal from a

single motor unit. The average force correlated with the impulses from the motor unit was measured in the usual way (Fig. IIB and C). Then the bipolar needle electrode was connected to a stimulator and stimuli having a duration of 0.1 msec were applied. Such brief stimuli tend to excite nerve branches rather than single muscle fibers. As the intensity of the stimulus was increased, all-or-none increments were recorded by the surface EMG which were similar in size to motor unit potentials recorded during voluntary contractions. Sometimes a small all-or-none twitch could also be seen by careful observation of the skin over the muscle. The response to stimulation at a low rate (less than 2/sec) could be averaged and the time course of the tension changes produced by the stimuli could be measured (Fig. IIA). In the absence of observable EMG responses no average tension changes were found. The average tension produced by stimuli strong enough to generate the first increment in the EMG represents the twitch tension produced by a single motor unit (Buchthal & Schmalbruch, 1970; Sica & McComas, 1971). Note the similar size and time course of the twitch tension evoked by stimulating a single motor unit and the average tension correlated with the spontaneous discharge of a motor unit in the same location in the muscle. On several occasions when stimulation was attempted, good agreement with the twitch tensions measured during a voluntary contraction was obtained (as in Fig. II). On other occasions the stimulated twitch did not agree with the average tension which was correlated with the discharge of motor units recorded at that site by the electrode during voluntary contractions. This variation in different experiments was expected since the nerve branch closest to the electrode may be the one going to

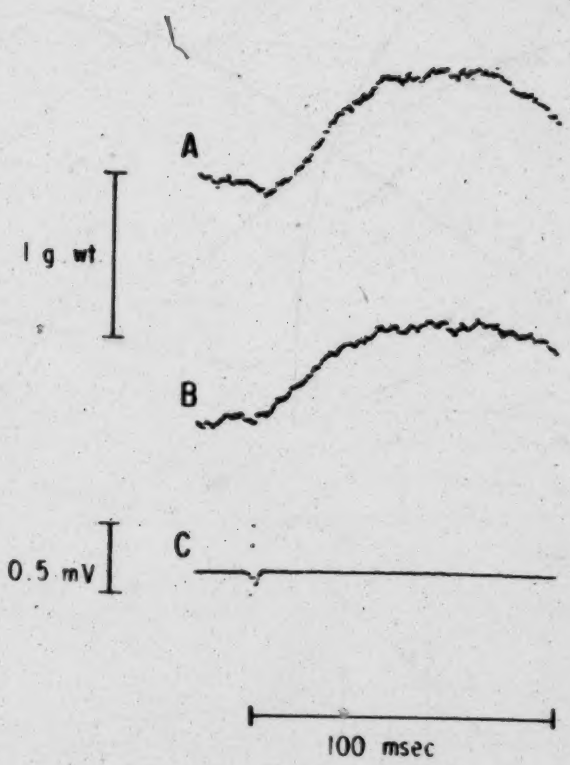

Fig. 11. Comparison of the average twitch (A) produced by stimulating a single unit and the average force (B) correlated with the impulses from a single unit (C) recorded at the same location in the muscle. The traces have been aligned so that the stimuli producing A occurred at the same point in the trace as the recorded impulses in C. Evidence is presented in the text that a single unit was being stimulated.

the motor unit being recorded or it may merely pass by the electrode to innervate a motor unit some distance away. However, if the average during voluntary contractions actually measured the tension produced by the nearly synchronous discharge of several motor units, the twitches produced by stimulating single units should often have been markedly smaller. No such difference between stimulation and voluntary activation was observed.

With further increases in the stimulus, other all-or-none increments could be seen. Fig. 12A shows the response to stimulating a small number of motor units when there was a minimal voluntary contraction. Fig. 12B gives the response to the same stimulus applied during a voluntary contraction of 350 g. The contraction time and the twitch tension are similar, but relaxation occurs more rapidly. The falling phase in Fig. 12B extends below the baseline before slowly returning to the original level. This phenomenon is probably a reflex effect as will be discussed later. Evidence that it was not purely mechanical in origin is presented in Fig. 13. The top trace shows that stimulating a few motor units in another subject also produced a contraction, then a relaxation below the previous level, followed by an oscillatory return to this level. The surface EMG was also being recorded in this experiment and is shown in the middle trace after rectification and filtering (see Methods in Chapter III). The two sharp peaks in the EMG (which actually go off scale) represent the stimulus artefact and the direct response to the stimulus. This response produced a small additional force of just over 2 g with a contraction time of about 40 msec. Each successive maximum or minimum in

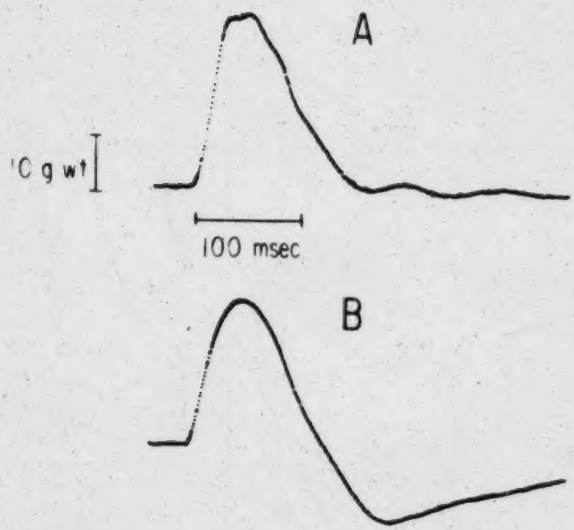

Fig. 12. Comparison of the average tension produced by stimulating at 1.7 c/s before (A) and during (B) a voluntary isometric contraction of 350 g. Note the more rapid relaxation and undershoot in B. The left edge of the time scale indicates the time of stimulation.

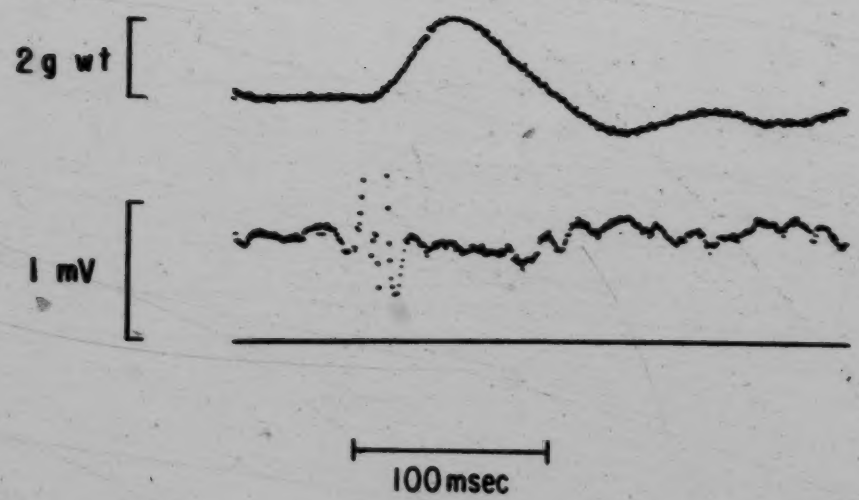

Fig. 13. Average tension (top trace) and average rectified surface EMG (middle trace) produced by stimulation of a few motor units during a voluntary contraction of 400 g. The bottom trace is a reference zero for the rectified EMG. Note the 10 Hz oscillations produced in both the tension and the EMG following a contraction of only 2 g. Further explanation in text.

the tension follows a corresponding maximum or minimum in the surface EMG with a similar latency. The results shown in Figs. 11 to 13, irrespective of their interpretation, suggest (1) the values of twitch tension and contraction time obtained during voluntary contractions are reliable measures of the twitches obtained from single motor units; and (2) the measured values for half-relaxation time during voluntary contractions may underestimate the true values.

Correlation with the surface EMG: Although the stimulation studies above suggest that the early time course of the force generated by single motor units can be measured simply by averaging, the results are not conclusive. In fact, the oscillations produced by stimulation (Fig. 13) represent a slight tendency toward synchronization in the discharge of motor units. Therefore the correlation was measured during voluntary activity between the timing of impulses from single motor units and of impulses from the whole population of motor units recorded by surface electrodes. Typical results from two subjects are shown in Fig. 14. The waveforms recorded with surface electrodes (second traces from top in Fig. 14) were of longer duration than those from needle electrodes (top traces) as commonly observed. In Fig. 14A the peaks in the rectified (third) trace were coincident with and agree in magnitude with the occurrence of the waveform in the unrectified trace (see also Fig. 5 in Methods in Chapter III). However, for all six units of another normal subject (Fig. 14B) a period of increased activity was evident in the rectified EMG extending approximately 10 msec before and after the occurrence of activity in the unrectified trace. This

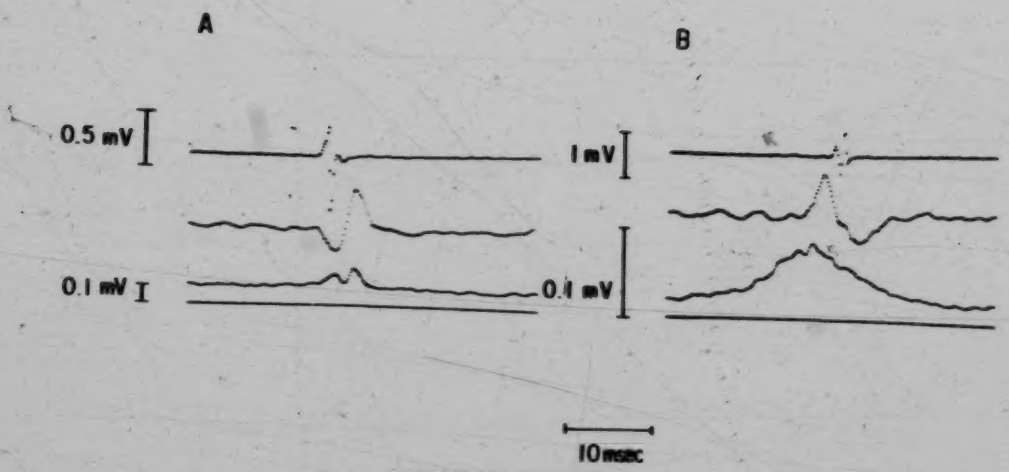

Fig. 14. Surface EMG associated with the impulses recorded by a bipolar needle electrode. The traces from top to bottom show (1) the average impulse from a single motor unit recorded by a needle electrode, (2) the average unrectified surface EMG associated with the impulses, (3) the average rectified surface EMG, and (4) a reference zero for the rectified signal. A and B are typical records from two different subjects. Note that the rectified surface EMG in B, but not in A, remains higher for about 10 msec before and after the occurrence of the impulses in the unrectified trace. This indicates that other motor units were tending to fire more often during this period in synchrony with the discharge of the motor unit recorded by the needle electrode.

indicates a tendency for other motor units to discharge near the time of impulses from the motor unit being studied. The force correlated with the discharge of single motor units in this subject was also several times larger at all force levels than in any other subject.

For forty-five units from six subjects we measured the area in the rectified EMG trace (see dotted area in Fig. 5) which was (1) above the steady level due to the ongoing activity of other motor units; and (2) above the voltage levels found in the unrectified trace. This extra area was expressed as a percentage of the area measured for the single unit on the unrectified trace (see Fig. 5B). In most of the subjects this extra area was minimal (well within the limits (< 10%) expected from partial summation according to Fig. 5). However, for the subject shown in Fig. 14B, the extra area was two or more times the area due to a single unit in five of the six units studied. We must conclude that in this subject there was a definite grouping of motor unit activity during normal isometric contractions. One other subject might have had a slight tendency for grouping of motor units. The extra area measured for eleven motor units in this subject was 19±3% (mean ± S.E. of the mean) which is somewhat higher than expected from partial summation.

Cross-correlations between motor units: The surface EMG and stimulation studies reported above indicate strongly that in most subjects the impulses from single motor units are remarkably independent of those from other units in the muscle. In other individuals, who can be identified by recording the surface EMG, several motor units may tend to discharge more or less synchronously. To get further insight into

the mechanisms involved in this synchronization, the cross-correlations between motor units recorded on two separate bipolar needle electrodes were measured (see Methods, Chapter III). This was done for eleven pairs of units in two subjects, one of whom had shown evidence of synchronization from the surface EMG recordings (Fig. 14B). A typical histogram for the cross-correlations between impulses from two units in this subject is shown in Fig. 15 (A vs B) together with the auto-correlation histograms for each unit separately. The autocorrelation histograms are often helpful in interpreting any periodicities observed in cross-correlation histograms (Moore *et al.*, 1970). The successive peaks in the autocorrelation histograms of Fig. 15 merely indicate the times at which the next and subsequent impulses occurred most commonly, measured from the time at which an impulse occurred to start the sweep. The cross-correlation histogram on the left of Fig. 15 is flat except for the obvious increase in a few bins just around zero time. Such an increase was observed in all five pairs of units examined from this subject, and again indicates the tendency for motor units to fire more or less synchronously. The implications of this result will be considered in the Discussion in Chapter V.

The second subject showed no significant correlations between the six pairs of units examined, although a small tendency for a peak near zero was observed in one or possibly two pairs of units (Fig. 15, C vs D).

Frequency response: Another important property of motor units and whole muscles is their ability to respond to fluctuating signals

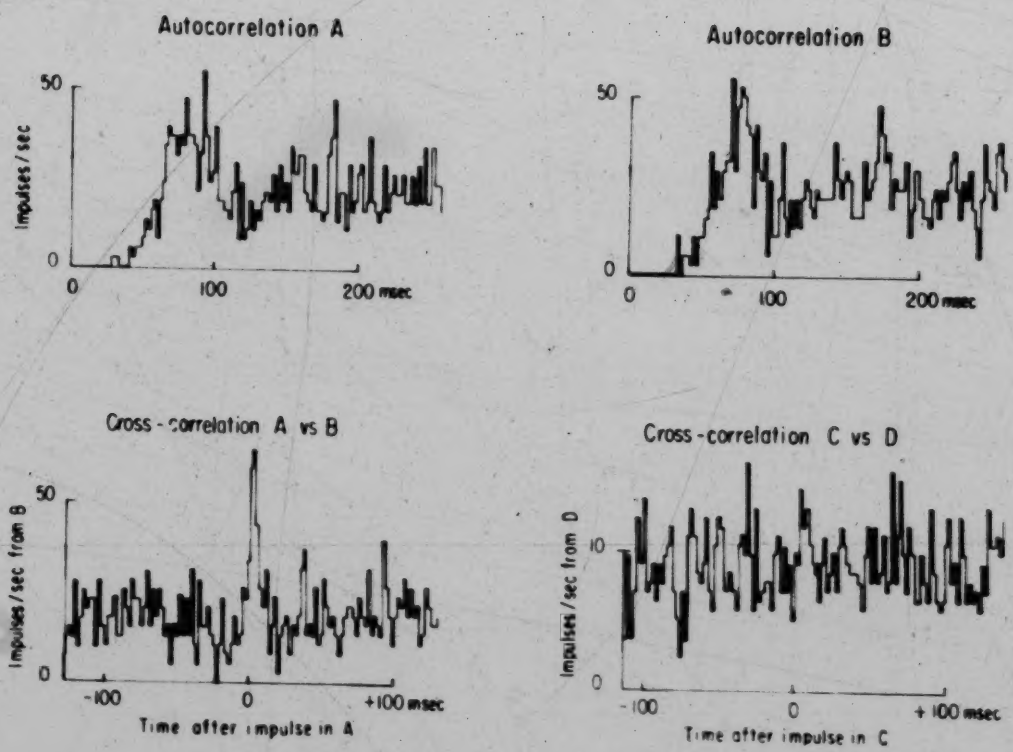

Fig. 15. Autocorrelation and cross-correlation histograms for pairs of units recorded simultaneously on separate needle electrodes. The autocorrelation histograms for units A and B have peaks at intervals where the next and subsequent impulses are generated following the impulses which begin the sweeps. The prominent peak near zero time in the cross-correlation histogram for these units indicates a tendency for impulses in the two motor units to occur nearly synchronously. Data from the same subject as in Fig. 14B and 15B. The cross-correlation histogram from another subject (units C vs D) showed, at most, a statistically insignificant peak near zero time. Further explanation in text.

which are found in normal behavioural movements and in tremor. The simplest way to predict the response of a linear system to signals of various frequencies is to take the Fourier transform of the response to a brief stimulus (impulse response). For a muscle the response to an impulse is the twitch, and the Fourier transform of the twitch can now be conveniently obtained using the Fast Fourier Transform algorithm (Cooley & Tukey, 1965). However, muscles show well-known non-linearities, such as a fused response to high (tetanic) rates of stimulation. Therefore, the frequency response obtained from the twitch may not be applicable to more natural conditions, where the motoneuron is producing a somewhat irregular series of partially fused contractions. Nonetheless, at various physiological rates of activity, linear models have been shown to account for most of the data obtained in experiments where muscles are stimulated with sinusoidally varying (Rosenthal *et al.*, 1970) or randomly varying stimulus trains (Stein *et al.*, 1972). The train of impulses produced naturally by a single motor unit during voluntary contractions contains a wide range of frequencies, and it is possible by spectral analysis to measure that part of the tension in the muscle which is linearly related to each frequency component contained in the train of impulses (see Methods, Chapter III). Therefore, the linear frequency response provides another way to compare at least the linear behaviour of motor units during stimulation and voluntary activity.

Fig. 16 shows the amplitude of the frequency response (often referred to as *gain*) for a single motor unit measured by spectral analysis on a log-log plot (Bode plot). The solid line is the curve

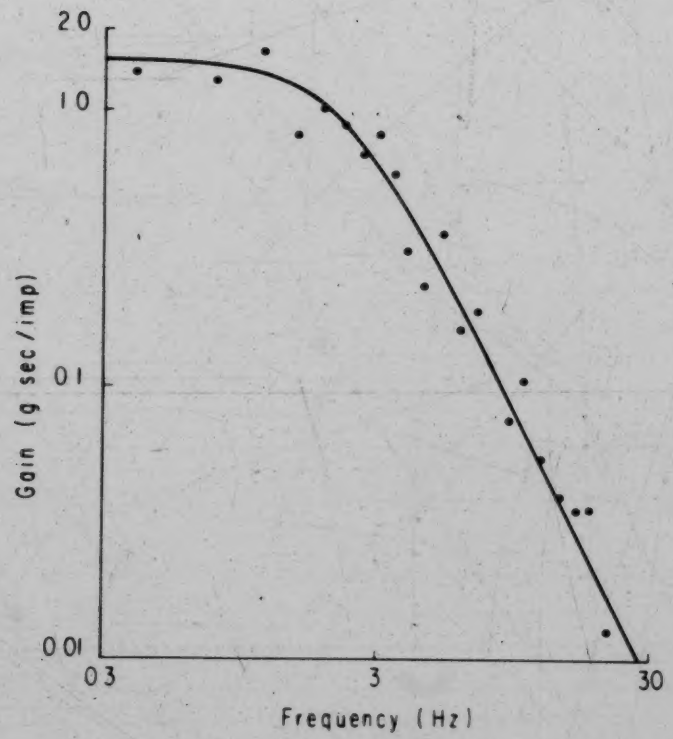

Fig. 16. Frequency response for a single motor unit during a voluntary isometric contraction. The gain measures the change in g for each impulse/sec modulation in firing rate of the motoneuron at the frequency indicated. The solid curve is the gain expected for a critically damped, linear, second-order system with a low frequency gain of 1.6 g-sec/impulse and a natural frequency of 3 Hz (D'Azzo & Houpis, 1966).

expected for a critically damped, second-order linear system (e.g., a suitably chosen mass, spring and dashpot would be an example of such a system). Three parameters which characterize a simple second-order system are its gain at low frequencies, G_0, it natural frequency, f_n, and its damping ratio, ζ (this ratio is 1 for a critically damped system). The other fitted values are given in the caption of Fig. 16. Note that the response amplitude falls off sharply beyond the natural frequency, even on a log-log plot. For a second-order system the slope on such a plot approaches -2, which indicates that the response amplitude falls off as $1/f^2$ at high frequencies. The gain is already reduced by more than an order of magnitude at a frequency of 10 Hz. These results indicate that the contractile properties of human motor units will be a strong factor in limiting the component of physiological tremor near this frequency (Schäfer, 1886; Hammond, Merton & Sutton, 1956; Lippold, 1970).

For twelve units recorded during voluntary activity the mean natural frequency was 2.4 Hz (individual values ranged from 1.4 to 5 Hz), and the mean damping ratio was 1.2 (values ranged from 1.0 to 2.0). In ten experiments one or more motor units were stimulated, and the frequency response was obtained from the Fourier transform of the twitch. The damping ratios were similar (mean = 1.2; range = 1.0 to 1.5), but the natural frequencies measured during stimulation were generally higher (mean = 5.6 Hz; range = 4 to 7 Hz). Both methods contain possible errors and limitations, so the significance of this difference is uncertain. It will be considered further in Chapter V.

IV.2 Recruitment of human motor units

Table I summarizes the measured values for the contractile properties of 145 motor units from the first dorsal interosseus muscles in the hands of three adult, male subjects.

Twitch tensions: The mean values for twitch tension are somewhat smaller than those found for extensor hallucis brevis of the foot (5.5 g; Sica & McComas, 1971), the only other human muscle which, to my knowledge, has been investigated in detail. However, the actual forces generated by the motor units will depend to an unknown extent on the series elasticity, the angle and the point of insertion of the fibers relative to the point of recording. Anatomical details were obviously not available for the subjects studied, but Feinstein *et al.* (1955) report that all muscle fibers in the muscle appear to run the entire length of the muscle.

More important than the absolute values is the histogram shown in Fig. 17A which gives the relative number of motor units with various twitch tensions. A wide range of twitch tensions was found, but small units were much more common than large units. Since the standard deviations (S.D.) of the observations in Table I are comparable to the mean twitch tensions, a nearly exponential distribution might be anticipated. This is a good approximation to the data, as shown in Fig. 17B. Because of the small numbers of large motor units, the data were grouped into increasingly large bins in Fig. 17B at high twitch tensions. (For the purposes of curve fitting the standard deviations of all points should be comparable.) The fitted line indicates that the

TABLE I

Subject	Twitch Tension (g)	Contraction Time (msec)	Half-Relaxation Time (msec)	Recruitment Threshold (g)
R.B.S.	1.36 ± 1.56 (64)	51.5 ± 12.6 (43)	42.8 ± 10.3 (22)	269 ± 309 (68)
R.Y.	1.31 ± 1.44 (45)	55.6 ± 11.4 (42)	44.9 ± 14.6 (16)	493 ± 460 (46)
A.M.	2.26 ± 2.8 (29)	59.1 ± 16.9 (29)	40.5 ± 7.7 (6)	352 ± 346 (31)

Contractile properties of motor units for three subjects. In each case the mean ± S.D. of an observation is listed with the number of observations (N) in brackets.

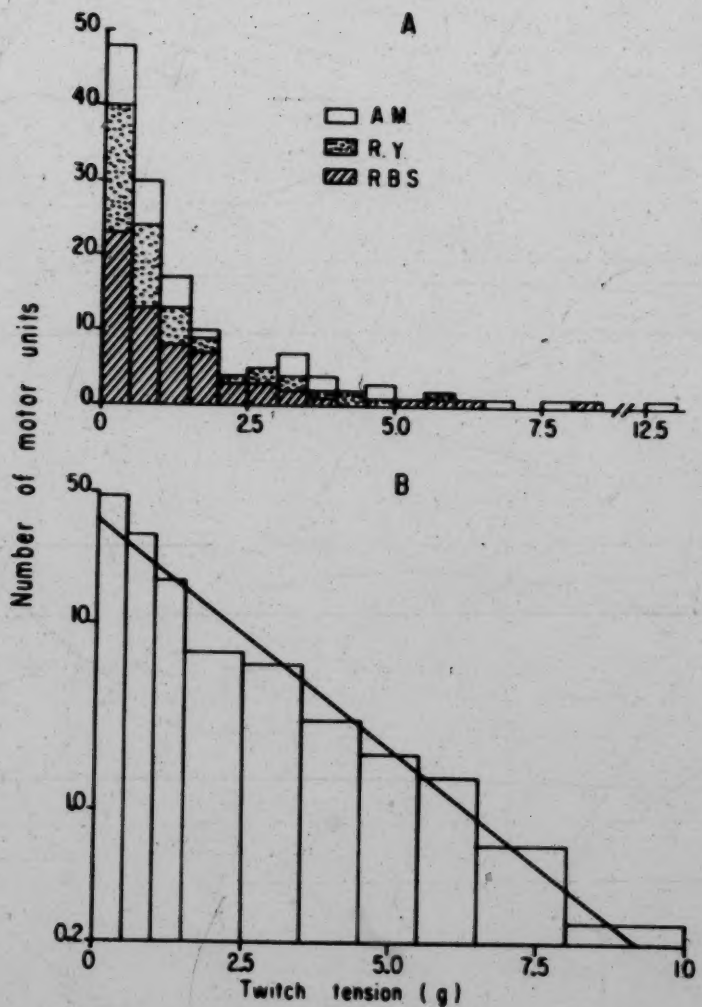

Fig. 17. Number of motor units, plotted on a linear scale (A) and on a logarithmic scale (B), having the twitch tensions indicated. The numbers from each of the three subjects are indicated on Fig. 17 and Fig. 18. The distributions are similar for all three subjects. The computed best fitting line on the semi-log plot of B indicates an approximately exponential relation between number of motor units and twitch tension.

probability of finding motor units of a particular size is halved for every 1.2 g increase in twitch tension. A similar, highly skewed histogram was found by McPhedran *et al.* (1965) for medial gastrocnemius muscle of the cat. More symmetrical histograms were obtained by stimulating motor axons to soleus muscle in the cat (Wuerker *et al.*, 1965) and extensor hallucis brevis in man (Sica & McComas, 1971).

Fig. 18A shows a histogram of the number of additional motor units which were recruited within a range of 100 g at different levels of voluntary contraction. A wide range is again observed, but the largest number were recruited at low force levels. Over half of the units were recruited at below 200 g, even though with the fixation used (see Chapter III), the subjects could exert well over 2 Kg (the maximum force measurable with the transducer). The significance of this distribution, which is similar to that found during reflex stimulation in cats (Henneman, Somjen & Carpenter, 1965) will be discussed later in Chapter V.

Individual values of twitch tensions for motor units from one subject are plotted in Fig. 19 as a function of the threshold force for recruiting each motor unit. Both variables cover roughly a hundred-fold range, and logarithmic coordinates have therefore been used for both ordinate and abscissa. The best fitting slopes for these plots (in the sense of least mean square deviation) were close to unity for all three subjects (mean slopes ± S.E. of the mean were 0.945±0.065, 0.922±0.086 and 1.04±0.12). This indicates a nearly linear relationship between twitch tension and threshold force over this entire range. The linear correlation coefficients were all greater than 0.8 which is

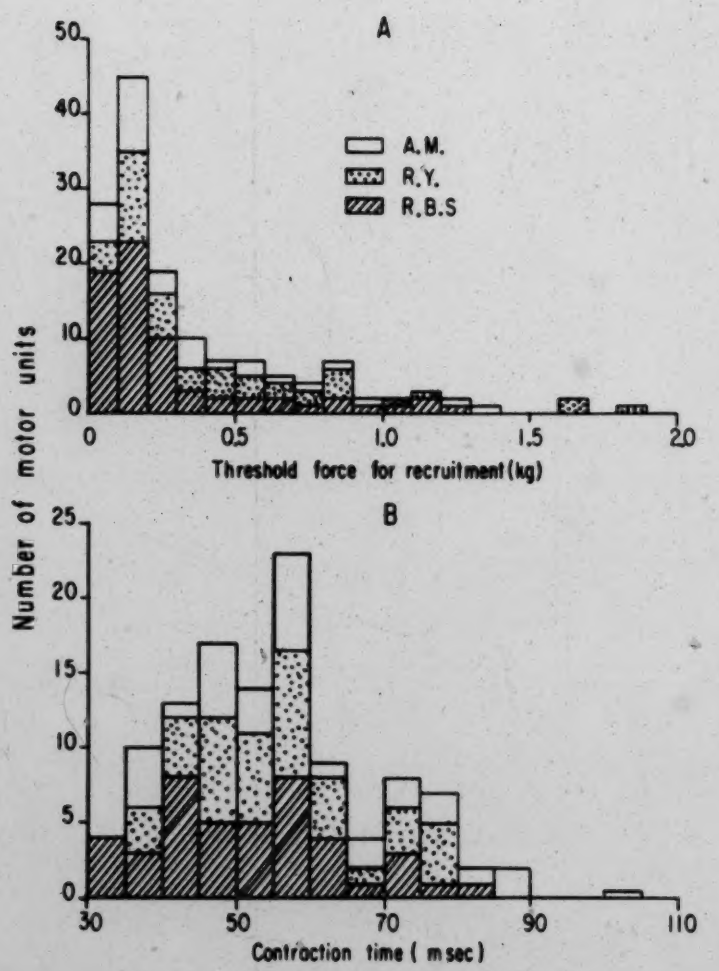

Fig. 18. Histograms of the numbers of motor units which were recruited at different levels of force (A) and which had the contraction times shown in B.

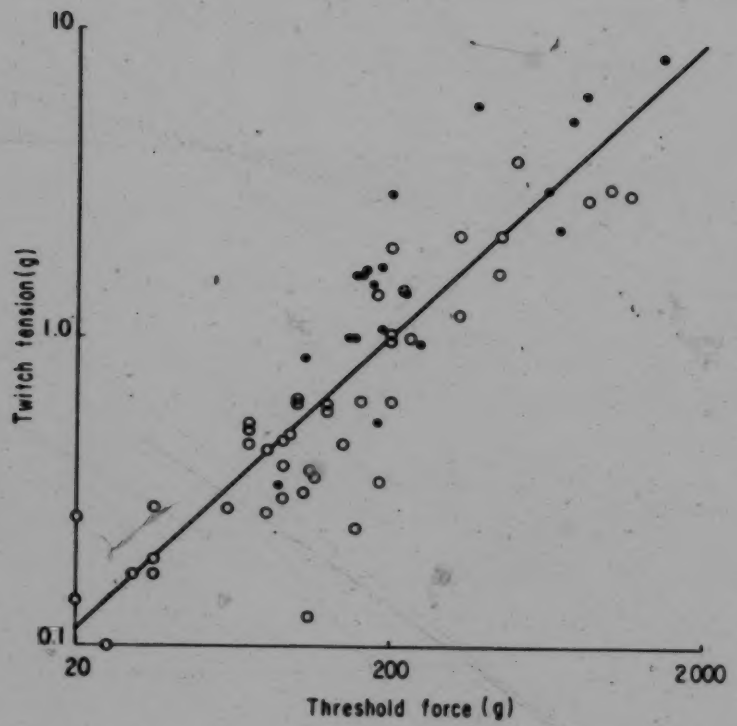

Fig. 19. Twitch tensions produced by single motor units in one subject (R.B.S.) as a function of the force at which the motor units were recruited. The filled circles in Fig. 19 and Fig. 20 are measurements from single experiments. The computed best fitting straight line shown on this log-log plot had a slope close to unity, indicating a nearly linear relation between these two variables.

highly significant. Thus, there appears to be an orderly recruitment of successively larger motor units during increasing human voluntary contractions, as has been found during reflex studies in animals (Henneman, 1968). This orderly recruitment has been observed in all normal subjects examined (more than thirty) to date.

Time course of the twitch: Fig. 18B shows a histogram of the number of motor units with different contraction times. The range of contraction times was from 30 to 100 msec in these subjects, and the mean contraction times in Table I were close to the values obtained by single maximal stimuli applied to the muscle (between 55 and 60 msec). No clear division between fast and slow twitch motor units was found, but over 80% of the units had contraction times less than 70 msec, and might be classified as fast twitch motor units (Sica & McComas, 1971).

There was a definite tendency for the first units recruited (Fig. 20A) to contract more slowly than those recruited at higher levels of force. The fitted straight line for this subject had a linear correlation coefficient of 0.6 which was highly significant. Similar results, although with a somewhat weaker correlation, were obtained when contraction time was plotted as a function of the twitch tension developed by individual motor units. Some correlation would be expected from the observed relation (Fig. 19) between twitch tension and the threshold force for recruitment. The same trends were observed for the other two subjects, although the decline in contraction time with increasing threshold was only significant at the 5% level in one subject and was not significant in the other subject.

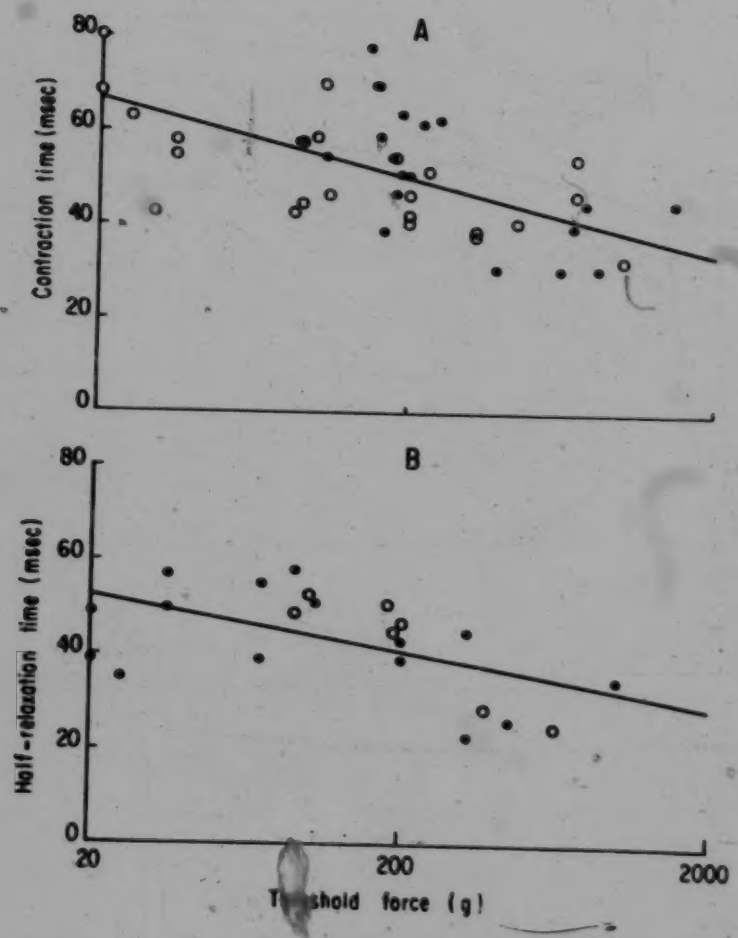

Fig. 20. Contraction times (A) and half-relaxation times (B) for single motor units in one subject (R.B.S.) as a function of the force at which the motor units were recruited. The computed best fitting straight lines on these semi-log plots had slopes significantly different from zero at the 1% (A) and 5% (B) levels of confidence.

Values for the half-relaxation times of motor units could only be measured for about 30% of the units studied using our techniques, and the values could have been influenced by several factors (enumerated in Section IV.1). Some tendency was observed for the units recruited at higher thresholds to have shorter half-relaxation times (Fig. 20B), but the best fitting straight line had a slope which was only significantly different from zero at the 5% level.

IV.3 Changes in firing rate of human motor units during linearly changing voluntary contractions

After determining the contractile properties and the threshold force for recruitment of a motor unit as described in the previous section, an attempt was made to measure the variation in firing rate of these units with the level of a voluntary contraction. Subjects were asked to apply sufficient force to track a triangular waveform displayed on an oscilloscope (see Methods, Section III.6). The force actually applied was measured by a stiff transducer and displayed continuously on the same oscilloscope for comparison. Fig. 21 shows a sample of the force applied by a subject in such an experiment, together with a continuous record of the interspike intervals and the measurements made from these records (see Section III.6).

Firing rate of motor units: Fig. 22 shows the averaged data, from over ten triangular waveforms, for firing rate as a function of force during a voluntary contraction. The symbols indicates by +'s represent the threshold values at which the units began and ceased to

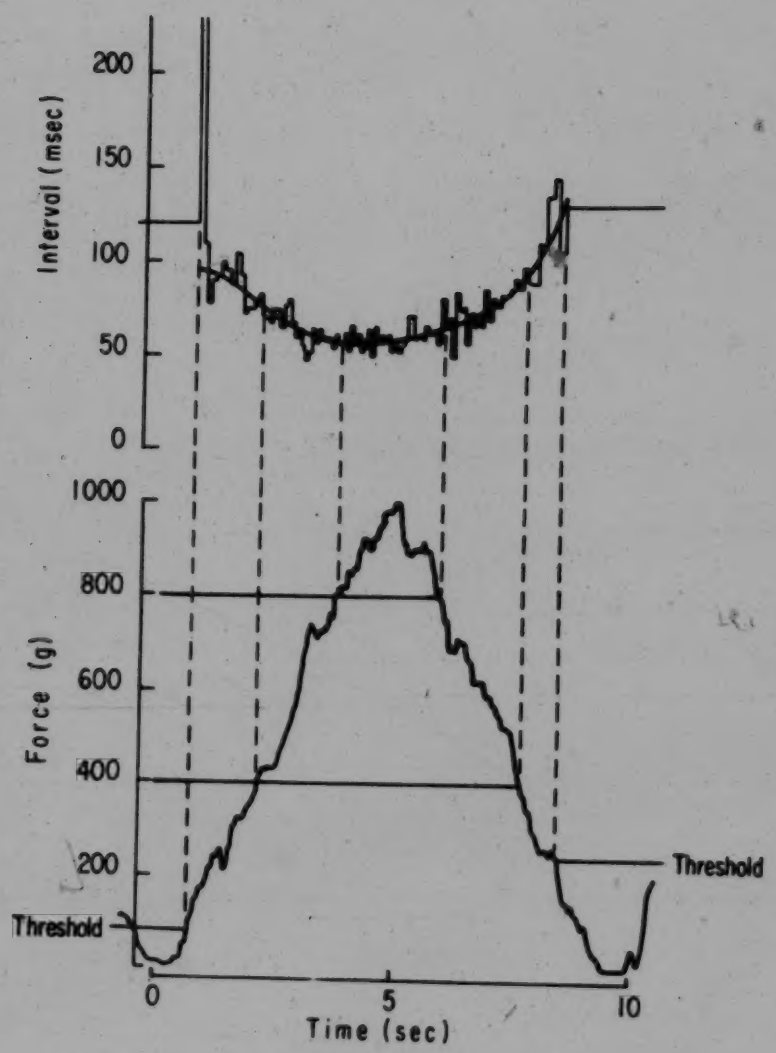
Interval (msec)
200
150
100
50
0
Force (g)
1000
800
600
400
200
Threshold
Threshold
0
5
10
Time (sec)

Fig. 24. Continuous record of interspike intervals from a single motor unit (upper tracing) and force (lower tracing) generated by the muscle in tracking a triangular waveform which required 1 Kg of effort. The interrupted lines indicate the measurements made, as indicated in the text, at threshold and at predetermined values of force (e.g., 400 and 800 g on the rising and falling phases of the force record. The value of interspike interval plotted on the pen recorder (to an accuracy of ±2.5 msec) is that of the preceding interval, so the last interval before the unit stopped firing is held, and a long interval (> 250 msec) is plotted as soon as the force surpasses threshold and the unit again begins to fire.

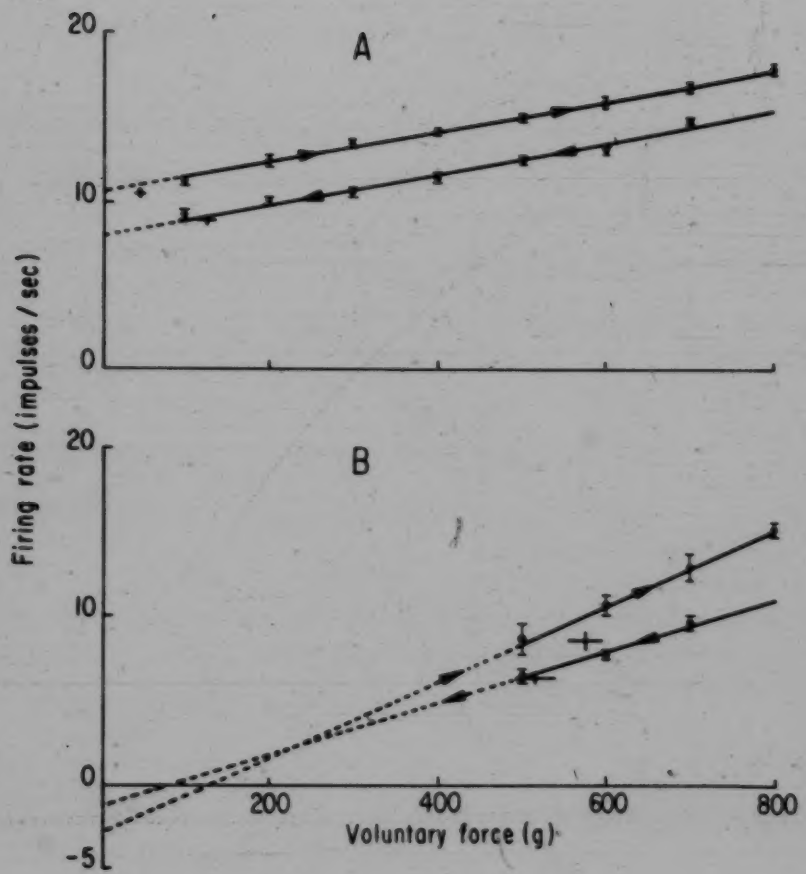
A
B
20
10
0
-5
200
400
600
800
Firing rate (impulses / sec)
Voluntary force (g)

Fig. 22. Firing rate of two motor units at threshold (+) and when passing predetermined force values (◆) during increasing (arrows directed upward to right) and decreasing (arrows directed downward to left) voluntary contractions. The extent of all symbols gives the standard errors about the mean values indicated from tracking over ten cycles of a triangular waveform. The straight lines were chosen to give the least mean square deviation from the data points at the predetermined force values. (Correlation coefficients all > 0.98.) The parameters used to specify these straight lines are the slopes and the firing rates extrapolated back to zero voluntary force. The firing rates at the intercept cannot, of course, be measured directly, because the units shown ceased firing at a mean threshold of (A) 90 g and (B) 545 g.

fire on average. Both units shown began to fire at a slightly higher rate than the rate observed just before they became quiescent (see also Clamann, 1970). This was true for twenty out of the thirty-one units studied; the mean difference was only 0.8 impulses/sec, but this was significantly different from zero at the 1% level of confidence. The average of the two measurements of threshold rate for all the units studied was 8.4±1.3 impulses/sec (mean ± S.D. of an observation). These values agree reasonably well with the "onset intervals" (142±39 msec) measured by Petajan and Philip (1969) for this muscle. The mean firing rate did not depend significantly on the threshold force at which the unit was recruited, although a dependence has been reported in adductor pollicis and abductor digiti minimi brevis by Bigland and Lippold (1954) and in brachial biceps by Clamann (1970).

Once they became active, both units shown increased and decreased their firing rate in quite a linear fashion as a function of the force generated by the whole muscle. The calculated best fitting straight lines are shown in Fig. 22 for the data from the rising and falling phases of the tension waveforms. Straight lines typically fitted the data extremely well (linear correlation coefficients were nearly all well above 0.9), though the best fitting line for the falling phase was often shifted (Fig. 22A) or had a somewhat different slope (Fig. 22B) from that for the rising phase.

These straight lines can be characterized by two parameters: (1) the slopes, which give the increase in firing rate for each 100 g increase in the force generated by the whole muscle; and (2) the intercepts, which give the rates of firing extrapolated back to zero force,

the region of extrapolation below the first data point for a particular condition is indicated by interrupted lines in Fig. 22. Fig. 23 gives the values of these parameters as a function of the threshold force for recruitment. Although the higher threshold unit in Fig. 22 has a steeper slope than the lower threshold unit, this trend is very weak in general and was not statistically significant. Units with all threshold values tended to increase their firing rate about 1.4±0.6 impulses/sec (mean ± S.D. of an observation) for each 100 g increase in the level of voluntary contraction.

A relation is seen (Fig. 23B) between the intercepts and the threshold level of voluntary force required to recruit a motor unit. As indicated in Chapter V, this relationship suggests that rate coding becomes increasingly important at higher thresholds. This hypothesis will be examined in detail later (see *Recruitment vs rate coding*), but first we must consider how the firing rates depended on the speed of contraction, and how effective these rates are in generating force. The next two sections deal with these questions.

Speed of isometric contraction: In contrast to the linear relationship between firing rate and isometric force observed, various non-linearities have been reported during nearly steady-state measurements (see Discussion in Chapter V). Therefore, it was necessary to determine what effects the speed of an isometric contraction had on the firing rates of single units. Subjects were asked to track triangular waveforms with different cycle times varying from 2 sec (0.5 c/s) to 50 sec (0.02 c/s).

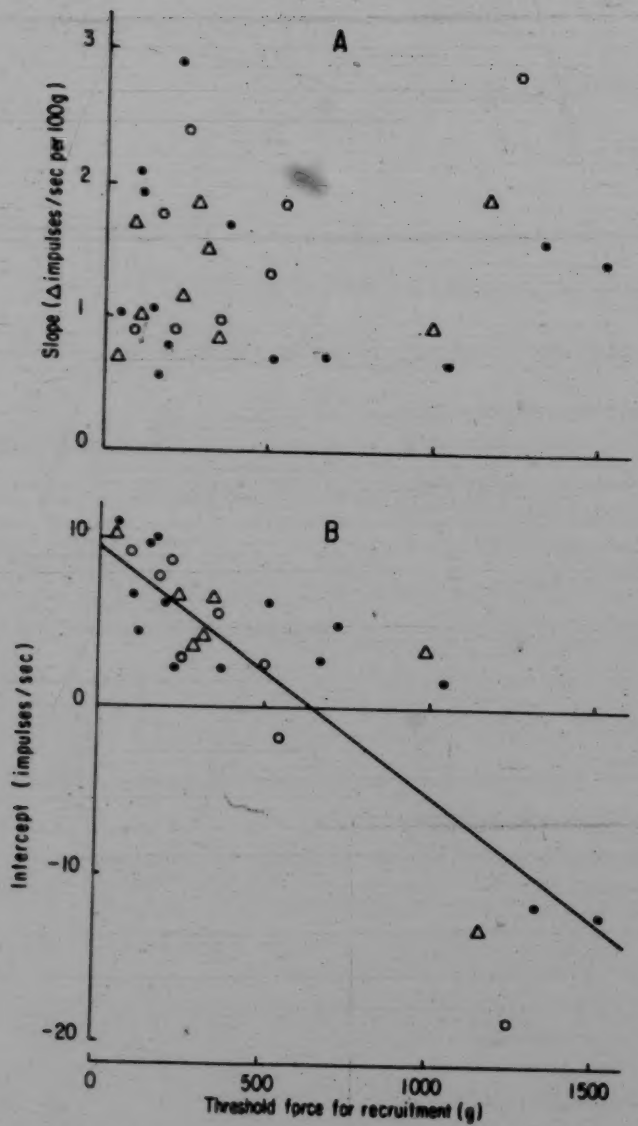

Fig. 23. Slopes (A) and intercepts (B) of best fitting straight lines (determined as shown in Fig. 22). Data for 31 units from the three subjects (indicated by different symbols) have been combined. The slopes did not change significantly with the threshold for recruiting a unit (correlation coefficient = 0.12), but the intercept did (correlation coefficient = 0.86). The implications of this result are discussed in the text.

Fig. 24 shows typical results for a single motor unit which was studied using triangles with three cycle times. Using the standard cycle time (10 sec), the firing rate increased quite linearly with force from its threshold near 600 g to the top of the triangular waveform at 1,600 g. However, with shorter cycle times the unit became active earlier and at a higher rate. Only beyond a value of 600 g did the firing rate increase substantially, and then to only slightly higher rates than those reached with the 10 sec cycle times. Thus, a positive curvature (second derivative > 0) is seen. A tendency for an initial discharge at constant rate, and the resultant positive curvature, was observed for each of the four units studied using waveforms with cycle times of 2 or 3 sec.

A different type of non-linearity was observed with long cycle times. The unit in Fig. 24 became active at a somewhat lower firing rate, and increased its rate rapidly until a "plateau" rate was reached (about 15 impulses/sec). A negative curvature (second derivative < 0), such as seen in Fig. 24, was observed in four out of the six units studied with triangles repeating every 20 or 50 sec. This type of non-linearity has been observed in many steady-state experiments (e.g., Bigland & Lippold, 1954; Dasgupta & Simpson, 1962; Clamann, 1970). Interestingly, neither non-linearity was as apparent on the falling phases of the triangular waveforms (Fig. 24B). If brackets indicating the standard errors about the mean values had been included, they would have overlapped considerably for all three repetition rates.

Motor units will become active at a lower force level than that at which they become inactive simply due to the fact that the

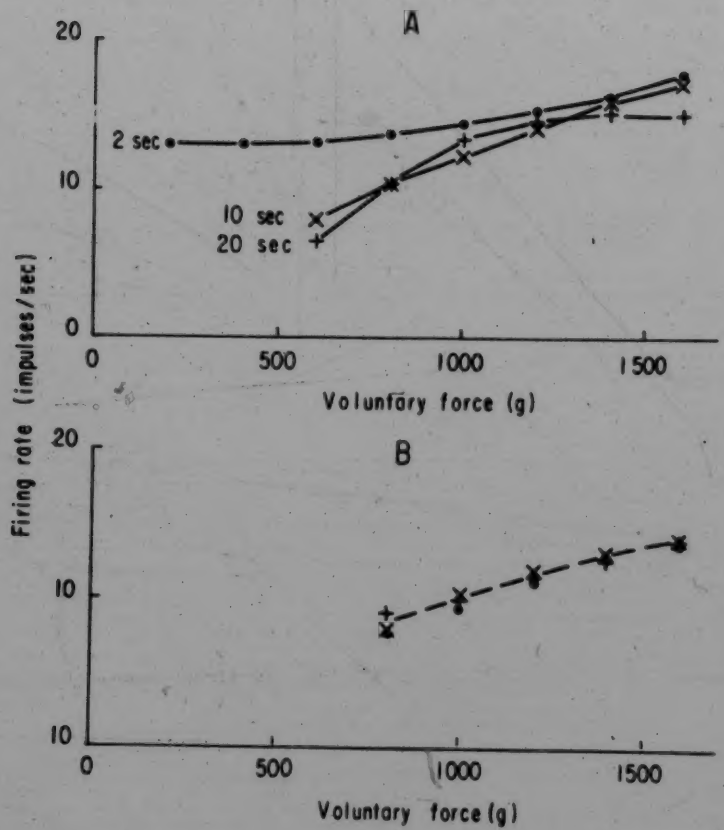

Fig. 24. Mean firing rate of a single motor unit during the rising (A) and falling (B) phases of the voluntary force produced by a subject while tracking triangular waveforms which repeated once every 2, 10 or 20 sec. The non-linearities seen in A with the shortest and longest cycle times are discussed in the text.

tension must inevitably lag the discharge of the motor unit by 50 to 150 msec, depending on the time course of contraction. These contractile delays become increasingly significant, the shorter the cycle time. However, the differences observed were often far longer than 50 to 150 msec, and could also be due to adaptation of the motoneurons (see Discussion in Chapter V). In the sample of thirty-one units studied, approximately 2/3 ceased firing at a higher force level than that at which they had become active. Despite the higher force levels on average, 2/3 also fired at a somewhat lower rate just before becoming inactive than their initial rate just after becoming active (see *Firing rate of motor units*).

Stimulation: To determine the effectiveness of various firing rates in generating force, the first dorsal interosseus muscles of two subjects were stimulated by means of (1) surface electrodes placed over the ulnar nerve; (2) surface electrodes placed directly over the muscle itself; and (3) a bipolar needle electrode (similar to those used for recording) which had been inserted into the muscle. Maximum voluntary contraction, against a stiff transducer capable of measuring up to 10 kg of tension, produced forces which agreed reasonably well with maximum tetanic stimulation of the ulnar nerve with brief pulses (0.1 msec). The maximum twitch produced by ulnar nerve stimulation was up to twice that generated by direct stimulation of the muscle, which suggests that up to half of the force recorded could have been generated by other muscles. However, direct muscle stimulation using longer pulses (2 msec) proved quite painful even at submaximal

levels, so we could never be certain that direct stimulation achieved full activation of the muscle.

Part of the muscle could be stimulated indirectly with little pain by inserting a needle into the muscle as described in Section IV.1. The needle was manipulated until part of the muscle could be stimulated selectively by a brief stimulus (0.1 msec) and a voltage less than 10 V. The needle presumably was then positioned close to a part of the nerve supplying the first dorsal interosseus muscle. The voltage was varied until a constant contraction was produced by each stimulus, and then various rates of stimulation were applied. At all times the surface EMG produced by the stimulus was monitored and data were only accepted if the surface EMG did not change in amplitude as the rate of stimulation was varied.

Fig. 25 shows the tension produced by different rates of stimulation applied intramuscularly. At rates up to 10 c/s the tension was relatively unfused. The peak-to-peak fluctuations in tension and the contraction were almost as large with stimulation at 10 c/s as at 1.7 c/s. This provides further evidence for the validity of the measurements of twitch tension and contraction time (Section IV.1) from the maintained discharge of a motor unit evoked voluntarily at rates below 10 impulses/sec. Fig. 25 also shows that the major increase in tension occurs at rates between 10 and 20 c/s with relatively little increase as the response becomes more fused at higher rates of stimulation.

Fig. 26 compares the force produced in a different subject by various rates of maximal stimulation applied to the ulnar nerve (Fig. 26A), or submaximal stimulation applied intramuscularly (Fig. 26B). In both

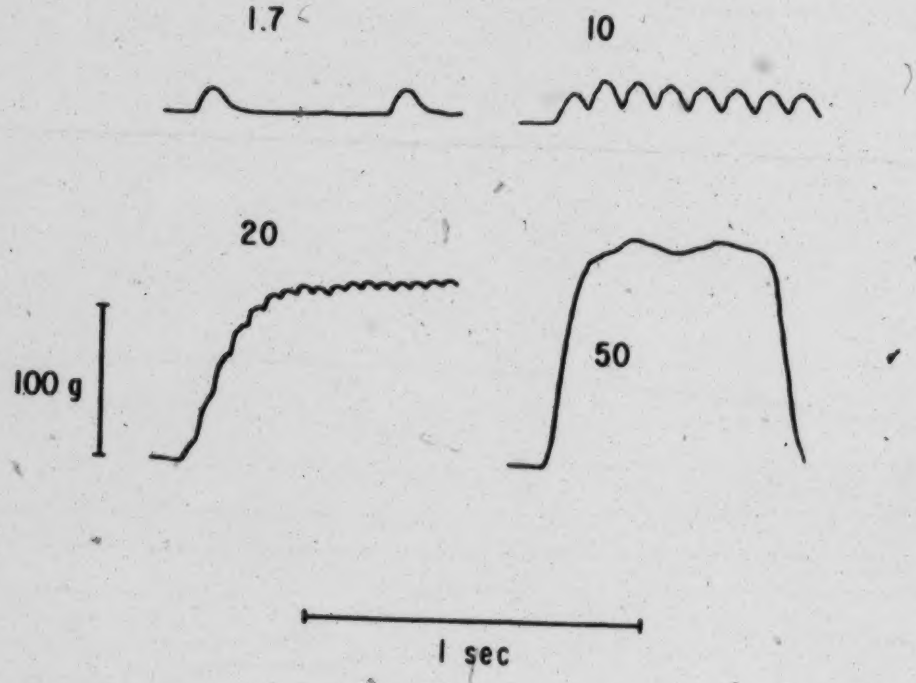

Fig. 25. Tension produced by submaximal stimulation at the rates in c/s indicated. The stimuli were applied through a bipolar needle electrode inserted into the muscle, and the EMG was monitored to ensure that the same number of motor units were being stimulated at each rate.

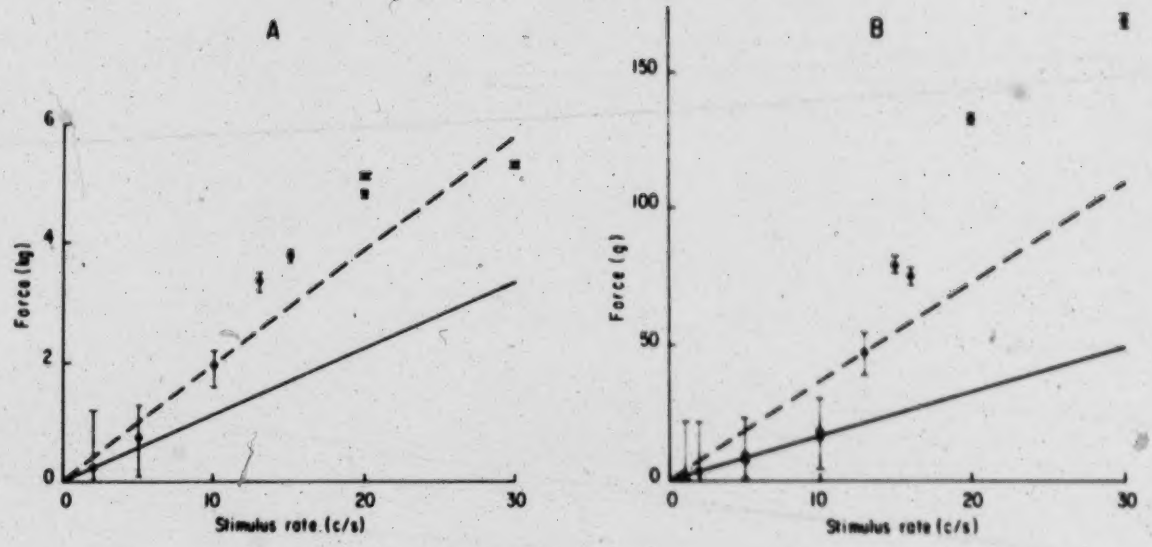

Fig. 26. Force generated by stimulating the ulnar nerve maximally (A) or by stimulating intramuscularly through a needle electrode (B). The vertical extent of the symbols represents the peak-to-peak fluctuations about the mean values indicated (filled circles). Several rates have been repeated twice. Two linear approximations to the data points (solid and interrupted lines) are described in the text, although the data appear to lie along a non-linear, sigmoid curve.

subjects tested the twitch/tetanus ratio was higher for ulnar stimulation (0.23, 0.19) than for intramuscular stimulation (0.13, 0.12). The sigmoid shapes of the two curves are otherwise similar despite the fact that the maximal ulnar nerve stimulation produced over thirty times as much force as the intramuscular stimulation via the needle electrode. Sigmoid curves of this type are generally found, although Bigland and Lippold (1954) were able to fit their data from human subjects by a straight line over most of the physiological range. Two linear approximations are shown in Fig. 26. The first (solid lines) is based on the area under the twitch in g-sec. If the muscle behaved linearly, each stimulus would produce an equal contribution and the force in g at any rate of stimulation could be obtained by multiplying the g-sec generated per stimulus by the number of stimuli/sec. This prediction is only fulfilled for stimulus rates up to 5 or 10 c/s. Above these rates the tension increases considerably faster until the tetanic tension is approached.

The second linear approximation (interrupted lines) assumes that the muscle can be treated as a critically damped second-order system. This has proven to be a good approximation during partially fused contractions for soleus muscle of the cat (Mannard & Stein, 1973) and for the present muscle as described in Section IV.1. The force expected can be computed if any two parameters of the twitch are known, e.g., the twitch tension and contraction time (see Section II.3). The second approximation appears to give a better fit to the data, but it may overestimate the force due to recruitment (which occurs at about 8 impulses/sec) and underestimate the changes due to rate coding over the normal, physiological range (8 to 20 impulses/sec) which represents the

steepest portion of the sigmoid curves of Fig. 26. This approximation will be used in the calculations of the next section, because of its simplicity, but the effect of any deviations from this approximation will be discussed (see *Stimulus rate-tension curves*).

Recruitment vs rate coding: The amount of force generated by the recruitment of previously inactive motor units during an increasing voluntary contraction can be calculated as follows. Let us divide the entire physiological range of forces into a number of segments, and consider the ith segment. We recorded from a number n_i motor units which were recruited in this segment, which spans a range x_i g. These motor units had a mean twitch tension P_i g and a mean contraction time T_i sec. Once recruited they began to discharge at a rate r = 8.4 impulses/sec which did not depend significantly on the segment i (see *Firing rate of motor units*) and did not vary significantly for any of the three subjects. According to the second-order approximation described in Chapter II (II.3), the tension-time integral generated by each impulse in a motor unit having a twitch tension P and contraction time T will be PTe g-sec where e = 2.72, the base of the natural logarithms. Thus, if each unit is recruited with the firing rate r, the total force y_i generated by recruitment of n_i units in the ith segment is given in g by:

$$y_i = n_i(P_i\ T_i\ e)r \qquad \text{IV.(1)}$$

$$= 23\ n_i\ P_i\ T_i$$

The force produced by increases in firing rate of motor units, which were already active before the increase in voluntary force of x_i g, can also be calculated. Consider the n_j units which were recorded from and which were recruited during the earlier jth segment. If these units had a mean twitch tension P_j and a contraction time T_j, they will produce an extra force of $n_j\ P_j\ T_j$ e g for each impulse/sec that their firing rate increases. We reported earlier (*Firing rate of motor units*) that all units increased their firing rate on average by 1.4 impulses/sec per hundred g or $\Delta r/\Delta x = 0.014$ impulses $\sec^{-1}$ g^{-1}. This value did not depend significantly on threshold, and no significant differences between subjects were observed. With an increase in force of x_i g the firing rate will increase $x_i\ \Delta r/\Delta x$ impulses/sec. The extra force due to this increased rate in those units previously recruited in the jth segment will be:

$$z_{ij} = n_j\ P_j\ T_j\ e\ x_i\ \Delta r/\Delta x \qquad \text{IV.(2)}$$

The total force in g due to all those units previously recruited will be:

$$z_i = \sum_{j=1}^{i-1} z_{ij} = e\ x_i\ \Delta r/\Delta x \sum_{j=1}^{i-1} n_j\ P_j\ T_j \qquad \text{IV.(3)}$$

$$= 0.038\ x_i \sum_{j=1}^{i-1} n_j\ P_j\ T_j$$

Thus, at each level of voluntary force, the percentage of extra force due to recruitment (e.g., in the ith segment this will be

100 $y_i/(y_i + z_i)$) and the percentage due to increased firing rate (100 $z_i/(y_i + z_i)$) can be computed for the population of units which we recorded from. For all three subjects (Fig. 27A) recruitment only accounted for the bulk of the force at low force levels. Although increasingly large motor units continued to be recruited at high force levels, they were few enough compared to the number of units already active, that the increased firing rate in the previously active motor units produced the bulk of the extra force. Over the range of contractions considered, which was only a fraction of the entire physiological range, increased rate produced about 2/3 and recruitment only about 1/3 of the total force accounted for (the percentages due to recruitment are listed for each subject in Fig. 27A).

Just by dividing the total force range into segments, the contribution of rate coding was also underestimated to some extent. Since the segments were quite wide (up to 500 g) at high levels of force, those units which were recruited early in the segment will have increased their firing rate considerably by the upper limit of the segment. Even at low force levels with the narrower segments, some rate coding will occur for each of the many units recruited within a given segment. This rate coding was not taken into account in calculating the results shown in Fig. 27. Had this been done, the forces in g due to rate coding would have been increased by about 10%.

Also shown in Fig. 27B are the percentages of the force accounted for by the two mechanisms (i.e., 100 $(y_i + z_i)/x_i$). Note that the percentages are roughly constant except at the lowest force levels. A variable amount of force, which was sometimes as much as 100 g,

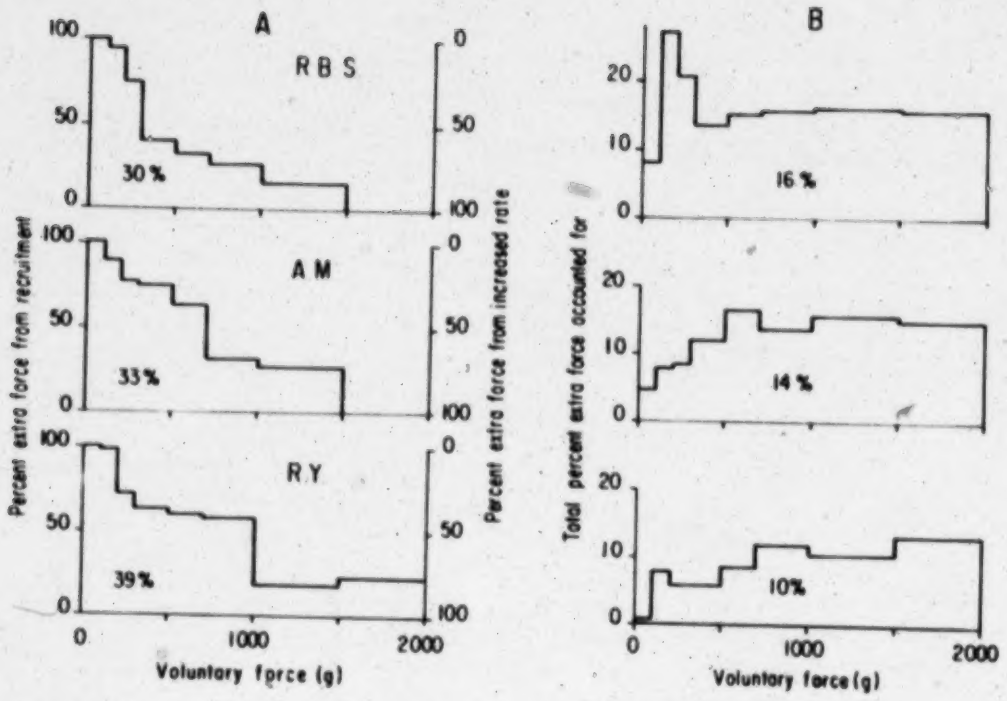

Fig. 27. A. Calculated percentages of force due to recruitment and rate coding for the three subjects at different levels of voluntary contractions. The overall percentage due to recruitment for the range studied (0-2 Kg) is listed for each subject. B. Calculated total percentages of force accounted for by the units studied at various force levels, considering both the mechanisms shown in A. The percentage accounted for in the entire range studied is also listed for each subject.

could be exerted simply by passively resting the finger against the transducer. This explains the lower percentages accounted for by active contractile mechanisms at the lowest force levels. The percentages are always considerably less than 100%, because only a fraction of the motor units in the muscle were sampled. The absence of substantial trends in the total percentages of force accounted for argues against substantial biases in the sample collected. For the three different subjects the highest percentages were obtained at low (R.B.S.), medium (A.M.) and high levels of force (R.Y.). The results from the subject A.M., who was unaware of the purposes of this experiment, fell between those of the other two. Knowledge of the experimental aims probably did not affect the results from the other subjects either, for it was only after completing the experiments and doing the calculations that the results emerged, and they were contrary in many ways to the results expected from the reading of the literature.

CHAPTER V

DISCUSSION (I)

In this chapter a discussion of the results obtained in Chapter IV will be presented. As in Chapter IV the discussion will be under three main sections: (1) The contractile properties of human motor units during voluntary isometric contractions; (2) Orderly recruitment of human motor units; and (3) Mechanisms involved in the gradation of voluntary contraction. The discussion on the abnormal motor unit studies will be presented in Chapter VII, following the Results (2) in Chapter VI.

V.1 The contractile properties of human motor units during voluntary isometric contractions

The results presented in Section IV.1 indicate that simply by averaging the force correlated in time with the discharge of single motor units, the early time course of contraction produced by the motor unit can be determined in many human subjects. In a few experiments (Fig. 11) it was possible to compare the average force associated with voluntary activation of a motor unit and the force produced by stimulation of a motor unit via the same needle electrode. Stimulation has been the only previous method (Buchthal & Schmalbruch, 1970; Sica & McComas, 1971) whereby the contractile properties of single motor units could generally be measured. Extreme care must be taken to ensure that only a single motor unit is being stimulated, whereas recording the electrical activity of single units is a well-known and routine

procedure.

Stimulation has the advantage that the full time course of a twitch can be studied, although when stimulation was superimposed on a voluntary contraction, an undershoot in tension was observed (Fig. 12). Determination of the time course by averaging voluntary activity is restricted by the minimum rates of firing normally generated (5 to 10 impulses/sec). The twitches are therefore partially fused, and it is sometimes not possible to measure the half-relaxation time of the twitch. However, the contraction times and twitch tensions measured were rather insensitive to the rate of firing over the range of rates examined. It was also noted that these parameters are not appreciably affected using stimulation of motor units at rates up to about 10 c/s. Those periods where the rate of discharge was slower than a preset value could be selected automatically (*Rate limitation*) to obtain a more complete twitch tension curve. However, rate limitation must be used with caution, because the slowest rates of firing tend to occur when the force in the muscle is slowly declining (Clamann, 1970). Therefore, with extreme rate limitation the twitch is superimposed on a downward-sloping trace (Fig. 10D).

Averaging the force correlated in time with the impulses of a motor unit during voluntary activity has the important advantage that the function of a motor unit can be associated with its contractile properties. However, this association can only be made if the impulses from one motor unit are not synchronized to those of other motor units. A strong one-to-one synchronization of motor units has only been reported in certain disease states (Lenman & Ritchie, 1970). However, a weaker

tendency for the impulses of motor units to occur in a group has been noted under various conditions (Buchthal & Madsen, 1950; Lippold, Redfearn & Vučo, 1957, 1960; Person & Kudina, 1968). However, Taylor (1962) could find no evidence that this grouping was due to mechanisms which synchronized the impulses of motor units. He could account for the observed grouping from the probability that various independent motor units might fire within a given time interval.

Using more stringent tests under the conditions of our experiments, the impulses from different motor units in most subjects were generated remarkably independently of one another. However, one subject showed a definite degree of synchronization, which was evident as a broad peak lasting ±10 msec, when the discharge of one motor unit was correlated with that of a second motor unit (Fig. 15) or with the whole population recorded by the surface EMG (Fig. 14). A brief increase around zero time would be expected in the cross-correlation histogram between two units if the units shared substantial common excitatory inputs (Moore *et al.*, 1970), for example, from higher centers or from muscle spindles. The second suggestion is consistent with the recent finding (Mendell & Henneman, 1971) that all motoneurons in a muscle may receive excitation from each muscle spindle afferent. Shared inhibition from Golgi tendon organs or from Renshaw cells would tend to produce a much broader peak in the cross-correlation histogram (Moore *et al.*, 1970). The relative lack of secondary peaks at the times of the peaks in the autocorrelation histogram also excludes the possibility that one unit was synaptically driving the other. This question of synchronization of motor units will be considered further

in Chapters VI and VII.

> "The common excitatory input received by two cells is reflected in a tendency toward synchronous firing that generates a peak near the origin of the postsynaptic cells cross-correlation. This is the "*primary effect*" of shared excitation, and obviously reflects the fact that the simultaneous appearance of EPSPs in both postsynaptic cells momentarily increases their probability of firing nearly simultaneously. Common inhibitory input tends to synchronize postsynaptic cell periods of nonfiring. This leads to the perhaps paradoxical result that, to the extent that their periods of nonfiring overlap, their periods of firing must also overlap, and hence they tend to fire in a synchronous, i.e., correlated way. A *broad* central peak is the only prominent feature in the cross-correlation histogram." (Moore *et al.*, 1970).

In other subjects, an undershoot in tension and EMG activity was observed, often followed by oscillations at about 10 Hz, when stimuli were applied which produced a contraction of even a few grams. This could also be a reflex effect due to an unloading of muscle spindles by the extra contraction. However, the role of Golgi tendon organs or Renshaw feedback cannot be discounted in the stimulation experiments. Marsden, Merton and Morton (1972) have recently shown that reflex gain does vary systematically with the level of voluntary contraction. One possible explanation of these results is that there are marked differences in the reflex gain used by different subjects doing the same task. High reflex gain would be desirable to maintain a given position accurately, but carries the risk of producing damped oscillations at about 10 Hz

such as occur in tremor (Lippold, 1970). An absence of tremor and associated synchronization of motor units would be desirable for producing a finely graded, smooth voluntary contraction. The magnitude of the tremor component near 10 Hz is well known to vary in different subjects and to depend on the level of voluntary effort (Sutton & Sykes, 1967).

The frequency response of motor units studied both during voluntary contraction and by stimulation was well fitted by a linear, second-order model, although differences in natural frequency were observed using the two methods. A second-order model also fits the data obtained from stimulating soleus muscle of the cat (Stein *et al.*, 1972), and the natural frequency declines and the damping ratio increases in that preparation as the mean rate of stimulation is increased under isometric conditions. Thus, the difference in rate during voluntary activity (5 to 10 impulses/sec) and during stimulation (1.7 c/s) might account for the observed difference. The frequency response obtained from recording single units, measures the extent of the linear correlation between the train of impulses and the tension in the muscle at various frequencies. However, the method cannot distinguish cause and effect. It will measure linear correlations in tension produced by the motor units, *and* any fluctuations in the firing rate of the motor unit which are linearly correlated with the general fluctuations in tension of the muscle. Even though a motor unit does not become entrained to high frequency fluctuations in tension, its rate of discharge may vary with low frequency fluctuations. Such an effect could explain the differences observed in the frequency

response functions obtained by stimulation and by voluntary activation of motor units.

Using either method, the response of the contractile elements to fluctuations in neuronal firing rate with frequencies near 10 Hz was already about an order of magnitude lower than the response to low frequency fluctuations. This should be a powerful mechanism for limiting the component of physiological tremor near 10 Hz. Studies on neuronal models in which subthreshold inputs decay exponentially with time (Rescigno *et al.*, 1970) indicate that in the absence of neuronal variability, the discharge of neuronal models will always become entrained to cyclic inputs, and show a discharge pattern that will repeat indefinitely. The presence of neuronal variability (Stein & French, 1970; Stein, 1970) tends to disrupt these patterns, but the simplest pattern (i.e., where one impulse is generated per cycle of oscillation) is the most resistant to disruption. Motor units fire steadily over a limited range of rates (approximately 5 to 20 impulses/sec from data obtained). Motor units firing at rates very different from 10 impulses/sec will not easily become entrained to these oscillations. However, motor units firing close to this rate may become entrained. The magnitude of physiological tremor near 10 Hz would then be determined by the number of motor units firing at appropriate rates and the strength of reflex effects. The magnitude would be limited by the resistance of motor units firing at other rates to entrainment by the reflex effects, and the low gain of the contractile elements in muscle at the frequencies found in normal tremor. Further work is required to determine the relative importance of these factors in normal postural

tremor.

V.2 Orderly recruitment of human motor units

The results from Section IV.2 provide the first direct evidence that motor units are recruited during increasing voluntary contraction in an orderly fashion according to the size of contraction they produce. This evidence strongly confirms the "size principle" expounded by Henneman (1968) and his colleagues, based on animal experiments and on recording the size of motor unit potentials in man (Olsen *et al.*, 1968). Indeed the degree of ordering (Fig. 19) is remarkably high (linear correlation coefficients >0.8 for all three subjects and for more than thirty other normal subjects subsequently studied) when one considers that the recordings were made in experiments over a period of several months, and that there are inevitably many uncontrolled variables in human experiments. Since the size of unit recruited (ΔF) is proportional to the mean force level (F) over such a wide range, the fractional increments in force ($\Delta F/F$) produced by recruiting each unit will be constant (see also Merton, 1951). This result is reminiscent of the constant Weber functions ($\Delta S/S$) sometimes obtained when just-noticeable differences (ΔS) are measured at various stimulus intensities (S) in sensory experiments (Werner, 1968). For example, Weber functions, $\Delta S/S = K$, can be computed from the stimulus response of a first-order cutaneous afferent nerve fiber responsive to mechanoreceptor stimulation. However, the functional significance of this observation has been questioned, since the amplitude of force fluctuations is a decreasing fraction of the total force exerted against

a control level (Sutton & Sykes, 1967).

Considerable flexibility in the order that motor units are recruited in different tasks has been reported (Basmajian, 1963; Grimby & Hannerz, 1968, 1970). Typically, in these studies, a wide range of movements has been possible, while the very orderly pattern found here may only apply to simple movements where there is a strong synaptic input which is rather homogeneously distributed among the component motor units. In Section IV.3, experiments were described in which subjects generated nearly linearly rising and falling forces. The threshold for a motor unit could be measured under these dynamic conditions as well as under static conditions. Although the two measurements were highly correlated (linear correlation coefficient = 0.88), individual motor units were found which had thresholds differing by a factor of two or more. This is consistent with the finding of Grimby and Hannerz (1970) that the order of recruitment could be quite different in tonic and phasic reflexes.

There was a tendency for the larger motor units, which were recruited at higher levels of voluntary force, to have a briefer time course (Fig. 20), as is commonly found in animal studies (McPhedran *et al.*, 1965; Wuerker *et al.*, 1965; Burke, 1967). However, the correlations measured between contraction time and threshold were lower than those between twitch tension and threshold, and the trend was not statistically significant in one of the three subjects. However, the twitch tensions generated by this subject at a given level of force were only about half of those recorded from the other two subjects, so the signal-to-noise ratios in the averages were smaller. The range of contraction times (30

to 100 msec) is also considerably smaller than the range of twitch tensions (0.1 to 10 g) which would tend to make it more difficult to detect any relationship. In the only other human study to our knowledge on this question, Sica and McComas (1971) were unable to demonstrate a relationship between twitch tension and contraction time.

Another interesting result of this study is the rapid, nearly exponential decline in the number of additional motor units recruited with the larger twitch tensions or the higher threshold. If the additional number of motor units recruited declines exponentially as the level of a voluntary contraction is increased, while the twitch tensions of the extra units increase linearly, then it follows immediately that recruitment will account for less and less of the increases in force at high force levels. However, we only recorded from a fraction of the motor units in any individual so sampling biases are possible. These methods required that the steady discharge of a unit be recorded for several minutes, and it is notoriously difficult to resolve single units at the limit of voluntary contraction. Thus, our sample is biased in that we probably did not record from the highest threshold units. It would be interesting to repeat the experiments using stimulation techniques (Buchthal & Schmalbruch, 1970; Sica & McComas, 1971), where the tendency should be to excite the largest motor units preferentially. However, care was taken to minimize sources of bias as much as possible, and we restricted ourselves to a range of forces (up to 2 Kg) where we could consistently record single units. Yet, the trend of the histograms was obvious throughout most of this range. Very similar histograms for the number of motor units with

various twitch tensions (McPhedran *et al.*, 1965) and thresholds for recruitment (Henneman *et al.*, 1965) have been found in animal experiments. Moreover, Grillner and Udo (1971) found that 90% of the motor units in soleus muscle of the cat had been recruited by the time the active tension in a stretch reflex had reached 50% of its final value. It will be shown in the next section that the increased rate of firing from active motor units accounts for an increasing percentage of force at higher levels of voluntary contraction. This can only be true if recruitment becomes less important during increasingly strong voluntary contractions.

Results from a single muscle should obviously not be extrapolated too far. Nonetheless, the striking similarity of these results (during voluntary contraction of a small human muscle, which is used in manipulation) to those of Henneman (1968) and his collaborators (during reflex contraction of large, postural muscles in the cat) certainly suggests the presence of rather general principles.

V.3 Mechanisms involved in the gradation of voluntary contraction

It has been possible for the first time to quantify the forces due to recruitment and the forces due to an increased firing rate of active motor units (rate coding) during increasing voluntary contractions. The results were contrary to the impressions gain from reading the literature. To quote two recent examples, Clamann (1970) concludes that his work, "quantifies and expands on the common observation that, at low tension levels, frequency change is the chief means of grading tension, while at higher tension levels, recruitment is the predominant mechanism".

Person and Kudina (1972) state that, "Recruitment is undoubtedly the main reserve of contraction strength increase. However, the mechanism of frequency change is unsurpassed as far as precision and smoothness are concerned". Yet at low force levels where fine adjustments are made, recruitment proved from our calculations to be the major mechanism. Increased rate proved to be responsible for the coarser adjustments that are made at higher force levels. Considering the whole physiological range, rate coding seems the major mechanism as originally suggested by Adrian and Bronk over forty years ago. Furthermore, the results at the two extremes of tension can be supported virtually without experimentation.

Mechanisms operating during minimal and maximal contractions: In a completely passive muscle, recruitment is the only mechanism operative initially because there are no active units whose firing rate can be increased. Petajan and Philip (1968) measured the "onset interval" for the first motor unit recorded by a needle electrode and the "recruitment interval" (i.e., the interspike interval of the first unit occurring when a second motor unit just began to fire). For the first dorsal interosseus muscle, the firing rate increased from roughly 7 to 10 impulses/sec from onset to recruitment. Increases of 30 to 35% were found in many muscles which they termed the "range of control" by rate coding. How much smaller this range of control by rate coding at low tensions might have been if Petajan and Philip had considered the difference in interval between the onset of the first unit and recruitment of the next unit in the whole muscle, rather than among those few motor units in the region sampled by a needle electrode.

At the other extreme, if all the motor units in a muscle could be activated by nearly maximal voluntary effort, this force could only be increased further by increasing the firing rate of the active motor units (rate coding). Grillner and Udo (1970) (see also Henneman, Somjen & Carpenter, 1965) found that 90% of the units were already recruited by the time the tension generated in stretching soleus muscle of the decerebrate cat reached 50% of its final value. From their Fig. 1 it appears that they found no units which were recruited beyond 75% of the final tension. They attributed much of the extra force to the stiffness encountered when stretching a contracting muscle. However, in these experiments, the muscle was being held at a roughly constant length, but no units were measured in two of our subjects which had thresholds for recruitment between 1.5 and 2.0 Kg. In the absence of recruitment, extra force could only come from increased firing rates in active motor units.

Determining the relative importance of the two mechanisms at intermediate levels of force required a considerable amount of experimental work and calculations. Several assumptions and approximations were made at various stages which require further discussion. However, before considering these in detail, it is worth noting that the trend of these results can be deduced simply from the observed linear relations between firing rate and force (Fig. 22).

Firing rate as a function of force: If a straight line were measured which went through the origin (zero intercept), then the rate of firing and the level of contractile force would increase exactly in

step beyond threshold. A doubling of rate would occur every time the level of voluntary contraction was doubled. A positive intercept (Fig. 22A) means that the firing rate will less than double each time the force level is doubled, once threshold has been reached, while a negative intercept (Fig. 22B) means that the rate will more than double with a doubling of force. Since the values of intercept decreased continuously (Fig. 23B) for units recruited at increasing levels of force, this implies that rate coding should be more important with strong contractions than with weak ones, *even if* the same number of extra motor units had been recruited at each level of force.

Plateaus in firing rate: Many studies (e.g., Bigland & Lippold, 1954; Dasgupta & Simpson, 1962; Clamann, 1970) have reported that the firing rate of motor units reached a plateau as the level of voluntary force was increased slowly. However, Clamann (1970) noted a linear relation between firing rate and force, when subjects tracked triangular waveforms, as found here. Furthermore, using slower and slower waveforms (down to a cycle time of 50 sec), plateaus have been observed (Fig. 24A) which become increasingly prominent at the longer cycle times. However, the minimum firing rate also decreased in these experiments, so that the range of firing rates observed often actually increased with slower contractions and relaxations.

Initial firing at roughly constant rates: With faster cycle times of 2 or 3 sec, motor units fired faster, earlier in the cycle, and initially with a roughly constant rate. Recently, Gillies (1972) had

subjects track linear ramps up to a final maintained level of force. He observed that motor units would often fire faster during the ramp than during the static portion of the waveform. The units might even stop firing altogether if their static threshold had not been exceeded.

The initially constant rate might be attributed to a balance between increasing drive and motoneuronal adaptation. Since adaptation becomes less and less marked with time (Fuortes & Mantegazzini, 1962), adaptation might also account for the fact that the firing rate during the rising, but not the falling phase of force depended on cycle time (Fig. 24). Whatever the mechanism involved, this initial burst at a higher rate does limit the scope for rate coding, so this mechanism may be relatively less important during rapid contractions. Again, one could argue *a priori* that with the briefest movements, in which motor units only fire once or twice, rate coding can play no part. Very little change in discharge pattern was observed during relaxation (Fig. 24B), with the range of cycle times used.

Sampling bias: The possibility that our samples contained a smaller fraction of the units, which are normally recruited at high force levels, cannot be ruled out. However, this possibility was discussed in detail in Chapter IV, and reasons were given for thinking that substantial bias was not present in the range of forces studied. Furthermore, no systematic trends were observed in the total percentages of force accounted for by the units studied using the two mechanisms (Fig. 27B). To argue that the forces due to recruitment were substantially underestimated at high force levels, reasons would also have to

be given for thinking that the forces due to rate coding had been overestimated at these levels.

Nonetheless, with the number of units sampled (see Table I), somewhat higher percentages might have been expected at all levels of force. From the percentages listed in Fig. 27B, 200 to 400 motor units would be required to account for 100% of the force. The only published histological measurements (Feinstein *et al.*, 1955) indicated the presence of approximately 200 large axons in the nerve to the first dorsal interosseus muscle, and some of these were presumably Group I muscle afferents. This supports an earlier suggestion (*Stimulation*) that other muscles were probably also contributing some force. Other factors could also have affected the absolute values computed. For example, the absolute value of force measured in Fig. 26B at 20 c/s was nearly twice that expected from the linear approximation (interrupted line).

Stimulus rate-tension curves: When stimulating either the whole muscle via its nerve, or a part of it with intramuscular electrodes, a sigmoid relation was observed (Fig. 26) between tension and stimulus rate, as generally found (Adrian & Bronk, 1929; Cooper & Eccles, 1930; Rack & Westbury, 1969). For simplicity in the calculations, a linear approximation was used, which assumed that the muscle could be treated as a critically damped second-order system.

The predictions from this approximation were larger and fitted the data points in Fig. 26 better than those from an approximation based on the area under a twitch. The reason is that the relaxation phase

expected for a critically damped system is slower than actually observed during a twitch. The half-relaxation time for a critically damped second-order system is nearly 70% greater than the contraction time as shown in Section II.3, while the half-relaxation time of the twitches shown in Fig. 25 is less than the contraction time. However, Mannard and Stein (1973) have shown that repetitive activity at physiological rates slows the relaxation process markedly, and the critically damped approximation holds reasonably well at certain firing rates.

The important point for the present discussion is that the linear second-order approximation appears to overestimate the force due to recruitment and underestimate that due to rate coding (see *Stimulation* and Fig. 26). Thus, any deviations observed will strengthen the present conclusions concerning the relative importance of rate coding. The extent of possible errors is uncertain because there were quantitative differences (e.g., in the twitch/tetanus ratio) between the stimulus rate-tension curves with maximal and submaximal (intramuscular) stimulation. The differences may simply result from the submaximal nature of the intramuscular stimulation. Muscle spindle afferents were presumably also being stimulated and at rates of 20 or 30 c/s could well have activated other motoneurons not directly stimulated by the needle (Upton, McComas & Sica, 1971).

It is also of interest that the common rates of firing we observed (8 to 20 impulses/sec) agree very well with the range of stimulus rates over which the tension increases rapidly (from roughly 15% to 85% of its tetanic value). Indeed, the rate coding found during voluntary contractions seems well suited to use nearly the whole range

of forces which the muscle can produce. The higher firing rates sometimes observed in other limb muscles (Adrian & Bronk, 1929; Lindsley, 1935; Norris & Gasteiger, 1955; Marsden, Meadows & Merton, 1971) would add little to the steady force generated by this muscle.

Maximal voluntary contraction: The forces generated during maximum voluntary contractions were two to three times as large as the maximum range of forces normally studied (0 to 2 Kg). If the trends observed in Fig. 27 continued up to maximal voluntary contractions, clearly rate coding would account for considerably more than 2/3 of the total force produced. An upper limit on the total force due to rate coding can be obtained from the values given above. If by maximal effort all motor units had been recruited and had increased their firing rates from 8 to 20 impulses/sec, then from the stimulation results, the tension due to recruitment would be only 15/85 = 18%, rather than the 34% measured on average for our three subjects.

In conclusion, although there are a number of assumptions and approximations which could affect the values calculated, the total contribution of rate coding to the generation of force in this muscle may have been underestimated, rather than overestimated, and the role of recruitment seems mainly confined to the generation of force at the lower levels of voluntary contraction.

CHAPTER VI

RESULTS (2)

This chapter will present the results obtained from (A) five patients after surgical repair of a complete unilateral severance of the ulnar nerve; (B) fourteen patients with unilateral and four bilateral pressure or entrapment neuropathies affecting the ulnar nerve; and (C) eight patients with motor neuron disease (amyotrophic lateral sclerosis). In addition, results obtained from synchronization studies on abnormals, controls and weightlifters will be given, as well as data from reflex experiments which were performed on controls and weightlifters with the purpose of investigating any changes in the central nervous system resulting from weightlifting which might be related to synchronization.

The following contractile and electrical parameters of single motor units were systematically measured from the first dorsal interosseus muscle of both hands of all patients (the normal hands served as controls when the lesion was unilateral): (1) the 'threshold' level of voluntary force for recruiting a motor unit; (2) twitch tension; (3) contraction time; (4) half-relaxation time; (5) the peak-to-peak amplitude of the surface EMG; (6) the peak-to-peak duration of the surface EMG; and (7) the rectified and unrectified surface EMGs for synchronization studies. The results will be given under the following subsections: (1) Pattern of recruitment of motor units; (2) Contractile and electrical properties of motor units; and (3) Synchronization of motor units.

VI.1 Pattern of recruitment of motor units

Completely severed ulnar nerves:

Twitch tensions and pattern of recruitment: The order of recruiting motor units can be examined by plotting the twitch tension generated by a motor unit against the 'threshold' force at which it becomes active during a voluntary contraction. Figs. 28A and B are plots of twitch tension vs threshold force for two patients in an early stage of regeneration (~6 months), while Figs. 28C and D are typical plots of patients at an advanced stage of regeneration (~2 years after surgical repair) following complete lesions of the ulnar nerves by sharp objects. In Figs. 28A and B the mean slopes ± S.E. of the mean of the best fitting straight lines were 1.005±0.164 and 0.63±0.11 respectively, in the normal hands, with linear correlation coefficients of 0.864 and 0.88. These values show that there is an orderly recruitment of successively larger motor units during increasing voluntary contractions, as previously described in Chapter IV.

In the 'abnormal' hands, however, the slopes of the best fitting straight lines were not significantly different from zero at the 5% level of confidence. The linear correlation coefficients of 0.3 and 0.15 respectively were also not significant. Thus, it appears that besides the comparatively small size of the twitch tensions during the early stages of regeneration which might be expected, the pattern of recruitment of motor units during increasing voluntary contractions was random. The patient whose data are shown in Fig. 28B had regained about 50% of her strength in the abnormal hand, but was unable to use that hand in knitting; the randomness of her recruitment pattern

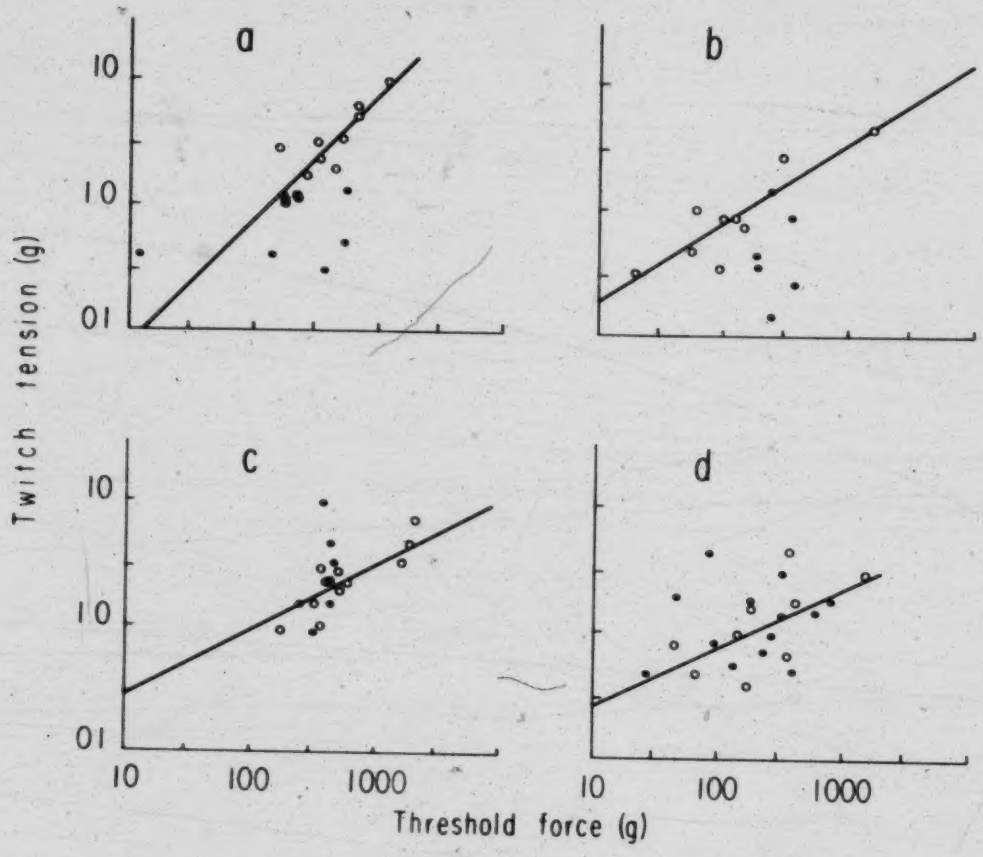

Fig. 28. Twitch tensions produced by single motor units from four patients with previous complete severance of their ulnar nerves as a function of the threshold force at which the motor units were recruited. (a), (b) - early stage of regeneration. (c), (d) - advanced stage of regeneration. The computed best fitting straight lines shown on these log-log plots are for the normal hands only. 0 - clinically normal hand; ● - affected hand.

could be partially responsible for this, as well as the possibility of anomalous re-innervation of the intrinsic hand muscles.

In Figs. 28C and D after two years of regeneration, the twitch tensions were approximately the same as the normal hand. However, the slopes of the best fitting straight lines were still not significantly different from zero and the linear correlation coefficients of 0.44 and 0.16 respectively were not significant. This clearly illustrates the fact that while the twitch tensions of motor units after regeneration can return to normal size, the normal orderly pattern of recruitment of motor units during increasing voluntary contraction was irretrievably lost.

Pressure or entrapment ulnar neuropathies:

Twitch tension and pattern of recruitment: Among the unilateral ulnar neuropathy patients, there was a tendency for the twitch tensions to be smaller in the affected hand but the normal orderly pattern of recruitment was still apparent in most patients. Fig. 29 shows two typical plots of twitch tension vs threshold force for two patients with ulnar neuropathies. In Fig. 29A the patient had recently developed an ulnar neuropathy associated with a partial block on conduction at the elbow, and recordings were made eight months after anterior transposition of the nerve. The slopes of the best fitting straight lines were 1.05±0.29 (normal), 0.7±0.15 (affected), the linear correlation coefficient in each case being 0.8. In Fig. 29B the patient had a ten-year history of ulnar neuropathy of uncertain etiology. The twitch tensions were approximately equal in both hands and the slopes

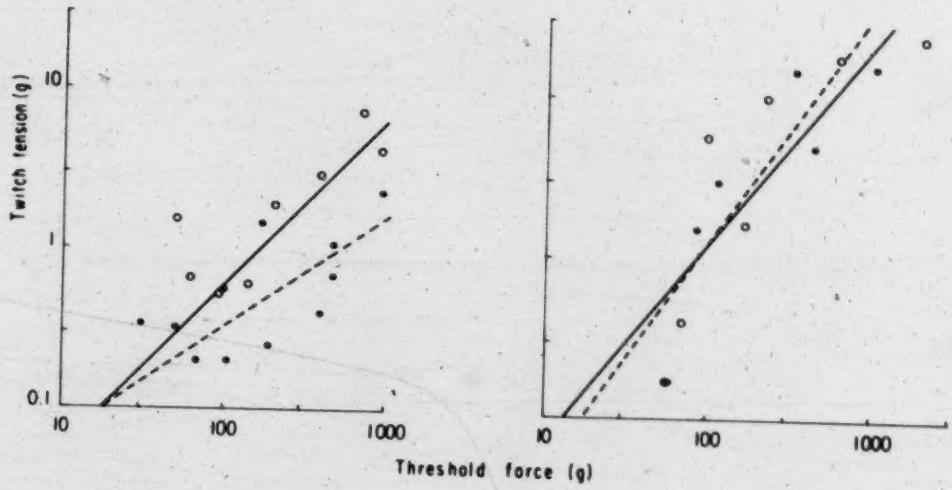

Fig. 29. Twitch tensions produced by single motor units, as a function of the threshold force at which the motor units were recruited from two patients with ulnar neuropathies. The computed best fitting straight lines (—— normal; --- affected) on these log-log plots had slopes significantly different from zero at the 5% level of confidence in both the normal and affected hands. 0 - clinically normal hand; ● - affected hand.

of the best fitting straight lines were 1.242±0.308 (normal), 1.425± 0.316 (affected): the linear correlation coefficients were 0.84 (normal), 0.86 (affected). These results indicate that the orderly pattern of recruitment of motor units is preserved.

Motor neuron disease: All of the patients in an advanced stage of this disease had few motor units so plots of twitch tension vs threshold force could not be obtained. Fig. 30 shows two cases in which enough units were recorded. In Fig. 30A the patient was unilaterally affected and the slopes of the best fitting straight lines were 1.02±.07 (normal), 1.357±0.161 (affected): the linear correlation coefficients were 0.97 and 0.94 respectively. The patient whose data are plotted in Fig. 30B was paralyzed in the right hand; units were recorded from only his weak left hand (power = 3 on a five point scale). The slope of the best fitting straight line was 1.287±0.21, with a linear correlation coefficient of 0.92. Thus, even though there is a general decrease in the number of motor units, the remaining motor units are recruited in an orderly fashion.

VI.2 Contractile and electrical properties of motor units

Pressure or entrapment ulnar neuropathies:

Twitch tension: Among the unilateral ulnar neuropathy patients, there was a tendency for the twitch tensions to be smaller in the affected hand. The overall means were 5.94±1.3 g (mean ± S.E. of the mean) for motor units in the normal hands and 3.66±0.69 g for motor units in the abnormal hands of fourteen patients. There was also a

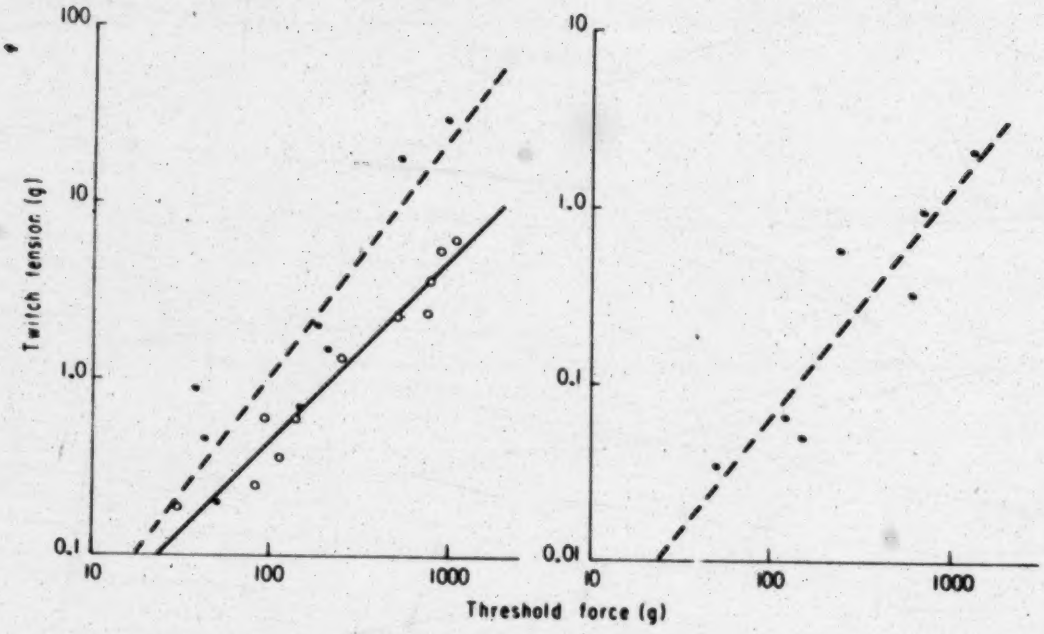

Fig. 30. Twitch tensions produced by single motor units as a function of the threshold force at which the motor units were recruited from two patients with motor neuron disease. The computed best fitting straight lines (___ normal; --- affected) on these log-log plots had slopes significantly different from zero at the 1% level of confidence in both the normal and affected hands. 0 - clinically normal hand; ● - affected hand.

general tendency for the contraction and half-relaxation times to be longer in the affected hands as illustrated in the histogram in Fig. 31. The mean values were 72±20 msec (mean ± S.D.) for the contraction times and 70±19 msec for the half-relaxation times of affected hands. The corresponding values in normal hands were 61±17 msec for the contraction times and 52±14 msec for the half-relaxation times. The distributions were significantly different ($P < 0.01$ for both parameters).

EMG amplitudes: The EMG amplitudes were generally larger (two times or more) in the affected hand. These results suggest the possibility of sprouting of healthy motoneurons to re-innervate the muscle fibers that had become denervated (Erminio, Buchthal & Rosenfalck, 1959; Wohlfart, 1957; Coërs & Woolf, 1959); the generally smaller sizes of the twitch tensions associated with these EMGs, however, suggests the involvement of other factors (see Discussion in Chapter VII). Fig. 32 shows the average of the twitch tensions recorded from the affected hands divided by the averages from the normal hands (twitch ratios). The corresponding ratios of the average EMG amplitudes of the affected and normal hands (EMG ratios [A/N]) are also given to illustrate the discrepancy between the relatively larger EMG amplitudes and the smaller twitch tensions. The distributions of the two ratios were significantly different ($P < 0.01$).

Motor neuron disease: Since seven out of the eight motor neuron disease patients were bilaterally affected, the EMG amplitudes and the twitch tensions recorded were compared with corresponding values

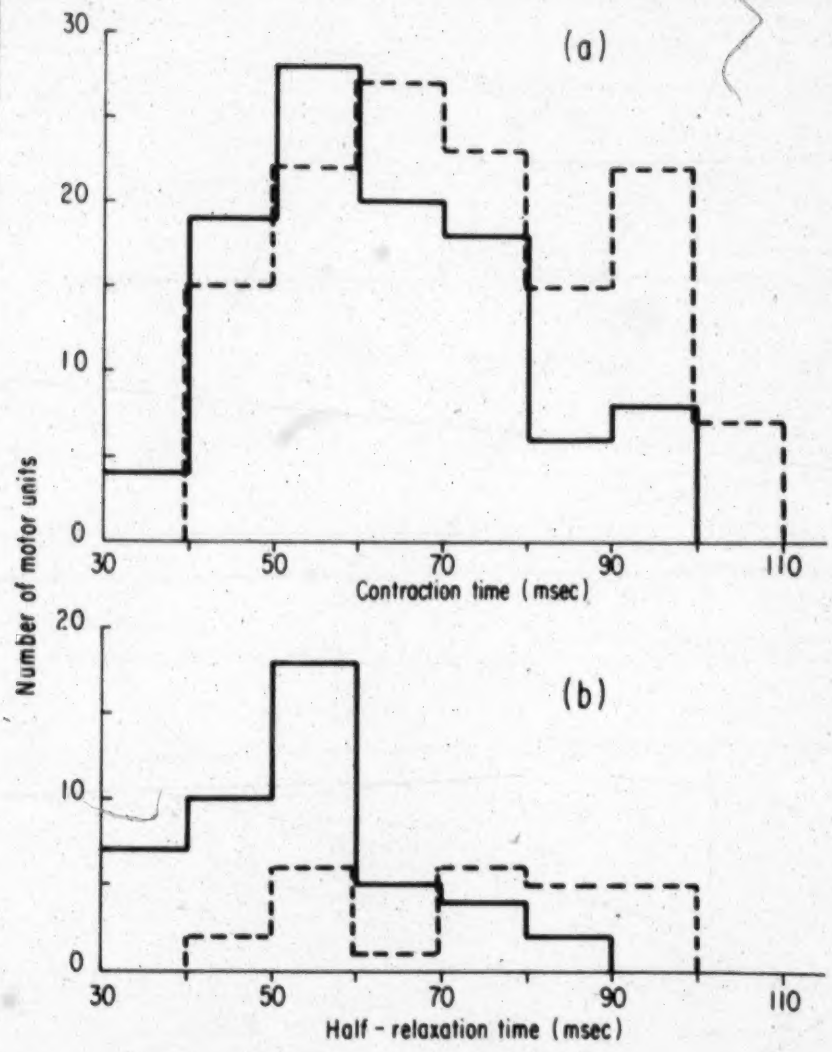

Fig. 31. (a) Contraction times of twitches from motor units in normal hands (continuous lines) and affected hands (broken lines) of fourteen patients with unilateral ulnar neuropathies. (b) Half-relaxation times of twitches from motor units in normal hands (continuous lines) and affected hands (broken lines) of fourteen patients with unilateral ulnar neuropathies. The distributions were significantly different ($P < 0.01$ for both parameters).

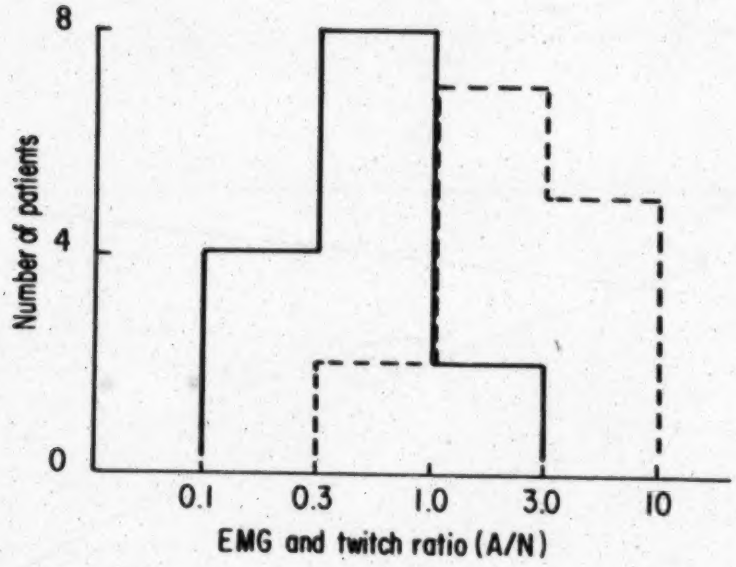

Fig. 32. Mean twitch tension ratios (continuous lines) and mean EMG amplitude ratios (broken lines) of affected (A) and normal (N) hands from fourteen patients with unilateral ulnar neuropathies. The distributions of the ratios were significantly different ($P < 0.01$).

pooled from twenty-five normal hands. Seven of the patients had larger EMG amplitudes (two to ten times normal average), but the twitch tensions were within the normal range. These large EMG amplitudes suggest collateral sprouting as has been previously reported (Erminio *et al.*, 1959). Fig. 33 shows histograms of EMG amplitudes and twitch tensions of normal and motor neuron disease patients. The mean twitch tensions of the normal and affected hands were 4.7±7.1 g (mean ± S.D. of an observation) and 4.5±6.9 g respectively; the distributions were not significantly different ($P > 0.8$). The mean EMG amplitudes of the normal and affected hands, 0.22±0.26 mV (mean ± S.D.) and 1.29±.149 mV respectively, had significantly different distributions ($P < 0.001$). This suggests that motor units enlarged by collateral sprouting are less efficient contractile units than units of normal physiological size.

The contraction times were longer in the affected hands (Fig. 34): the mean values of the contraction times were 78±21 msec in the affected hands and 61±17 msec in the normal hands and the distributions were significantly different ($P < 0.01$).

VI.3 Synchronization of motor units

The following results will be presented in this section: (1) The effect of ulnar neuropathies on the synchronization of motor units; (2) The effect of weightlifting on the synchronization of motor units; and (3) data from reflex experiments which were performed with the purpose of determining the cause of synchronization.

Synchronization ratios, as explained in Methods (Chapter III),

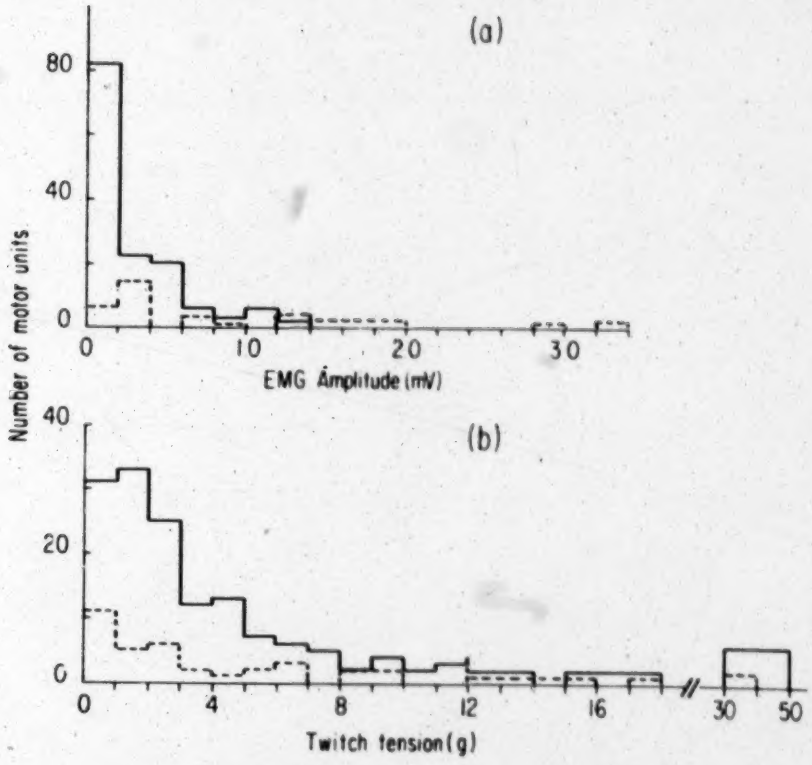

Fig. 33. (a) EMG amplitudes of motor units from twenty-five normal subjects (continuous lines) and eight patients with motor neuron disease (broken lines). (b) Twitch tensions of motor units from twenty-five normal subjects (continuous lines) and eight patients with motor neuron disease (broken lines). The distributions of the twitch tensions were not significantly different ($P > 0.8$), but the distributions of the EMG amplitudes were significantly different ($P < 0.001$).

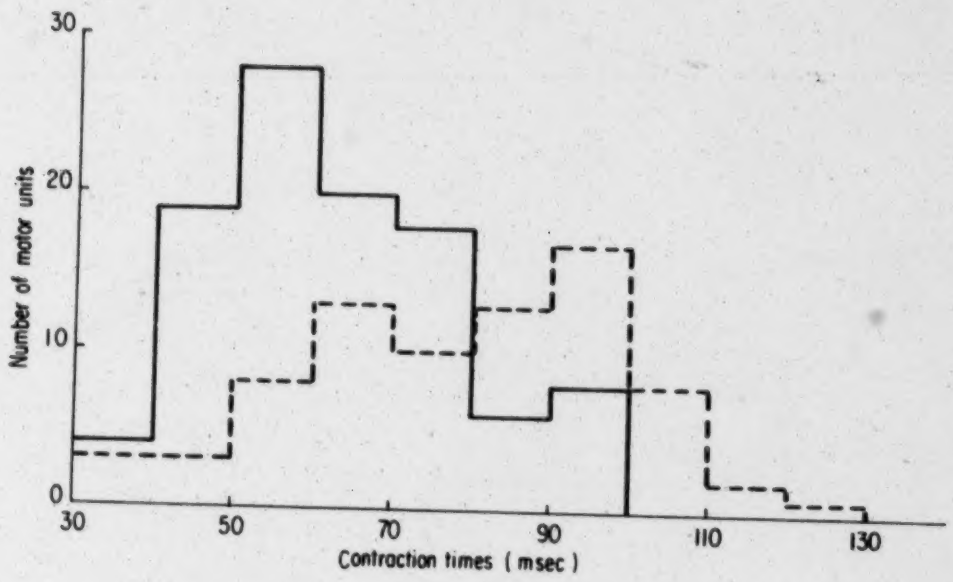

Fig. 34. Contraction times of twitches from motor units in twenty-five normal hands (continuous lines) and in eight patients with motor neuron disease (broken lines). The distributions of the contraction times were significantly different ($P < 0.01$).

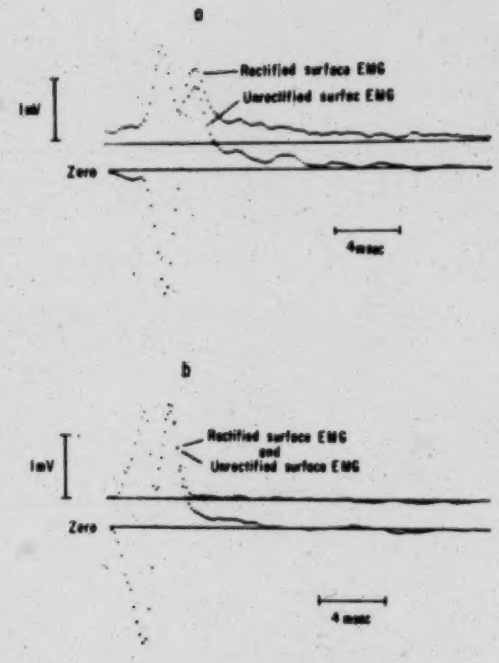

Fig. 35. Experimental traces of an averaged rectified surface EMG superimposed on an unrectified surface EMG, for evaluating synchronization ratios: (a) normal hand; (b) affected hand. Horizontal lines indicate voltages of zero and the mean rectified surface EMG.

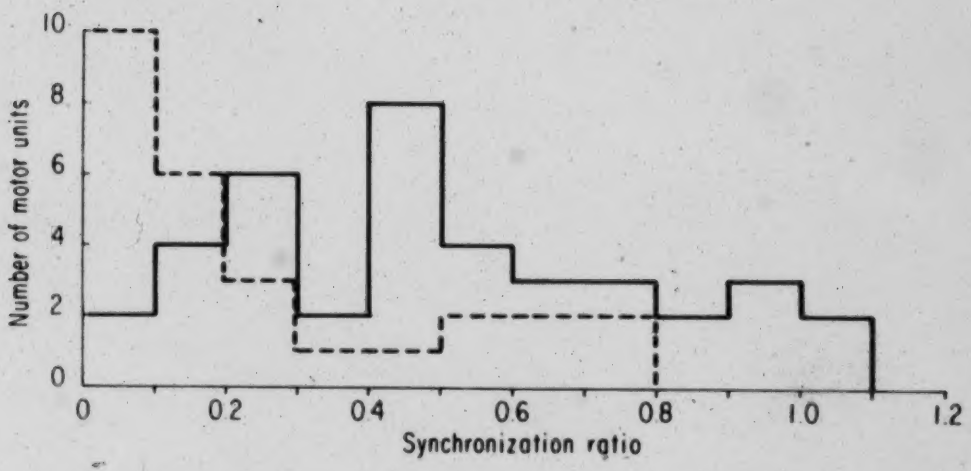

Fig. 36. Synchronization ratios of normal (continuous lines) and affected (broken lines) hands of five patients with ulnar neuropathies who showed synchronization. The distributions of the synchronization ratios differed significantly ($P < 0.01$).

were computed for all the patients with ulnar neuropathies. Fig. 35 shows experimental data of a rectified surface EMG superimposed on an unrectified surface EMG for one of the patients who showed synchronized motor unit activity - (a) normal, (b) affected. Only five of the patients showed synchronized motor unit activity in their normal hand; the effected hands showed either a decrease in synchronization or a complete absence of synchronization. Fig. 36 is a histogram of the synchronization ratios for the normal and affected hands of the five patients; 0.2 was taken as the lower limit for synchronized activity (see Methods' in Chapter III). All the patients in our sample who showed synchronized activity were men and most worked at manual jobs which required exertion of relatively large forces with these muscles. To test whether there was any connection between the regular exertion of large brief forces and synchronization, seven weightlifters were examined and all showed clear evidence of synchronization. Fig. 37 is a histogram of synchronization ratios of seven weightlifters and seven non-weightlifters. The distribution of the means were significantly different ($P < 0.001$).

In each subject the EMGs were recorded at different threshold forces for recruiting a motor unit. The threshold force varied from about 100 g to 2 Kg; the synchronization ratio, however, did not seem to depend on the threshold force. Fig. 38 shows two examples of synchronization ratio against threshold force (up to 1.5 Kg) of two subjects. There is obviously no correlation between the two parameters.

In an attempt to determine the nature of the mechanisms responsible for causing synchronization, reflex experiments were per-

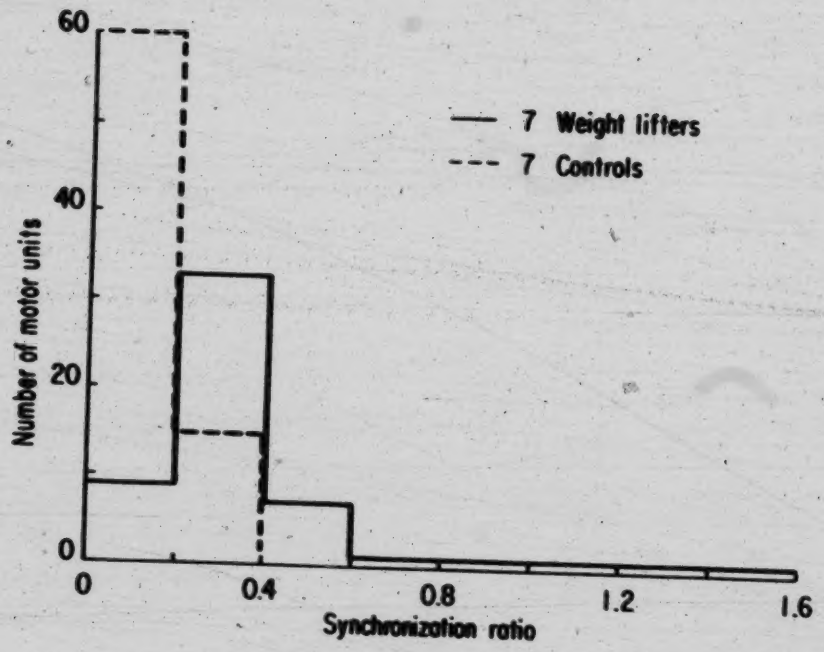

Fig. 37. Histogram of synchronization ratios of seven weightlifters and seven non-weightlifters. The distributions of the means were significantly different ($P < 0.001$).

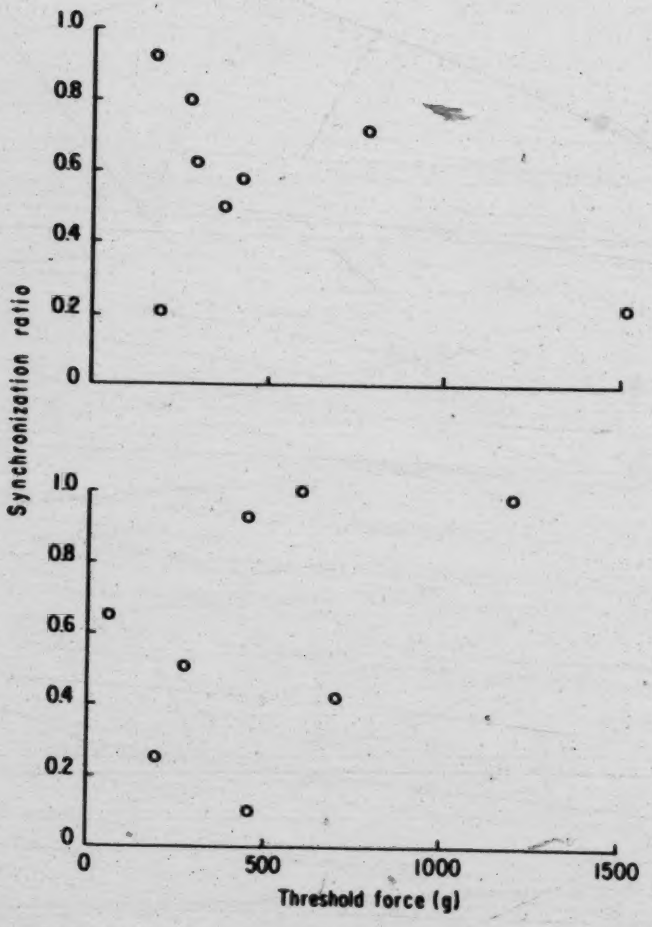

Fig. 38. Synchronization ratios against threshold force for recruiting a motor unit, from two subjects who showed significant synchronization.

formed on four weightlifters and five control subjects. These experiments involve stimulating the median nerve at the wrist with stimuli which are nearly maximal for α-motoneurons. EMG activity was recorded simultaneously from the abductor pollicis brevis muscle. Preliminary studies were done stimulating the ulnar nerve and recording from the first dorsal interosseus muscle. However, as reported previously by McComas *et al.* (1971), the reflexes in this muscle are much smaller. Simultaneously evoked potentials were recorded from the skin over the cervical spine, and from the scalp over the motor cortex (see Methods in Chapter III). Fig. 39 shows averaged EMG, spinal and cortical potentials when voluntary force was being exerted. The EMG was rectified before averaging and so shows double peaks. V_1 is the usual spinal H-reflex or monosynaptic reflex, of latency 30 msec, while the latencies of the later V_2 and V_3 waves suggest supraspinal and possibly cortical reflexes. The V_1 and V_2 waves were described previously by Upton *et al.* (1971) who introduced the letter *V* since these waves are greatly potentiated by volition, and are difficult to demonstrate in completely relaxed muscles. The V_3 wave has not previously been described and has been seen in all the weightlifters, but only in one control subject. The ratios of the peaks of the V_1 and V_2 waves to the maximum peak of the *M* wave were calculated for each subject. Fig. 40 shows histograms of these two parameters for both weightlifters and controls. The mean $\frac{V_1}{M}$ was slightly larger among the weightlifters (0.12±0.05 compared with 0.09±0.04) but the distribution was not significantly different ($P > 0.7$). The mean $\frac{V_2}{M}$ was, however, twice as large among the weightlifters (0.1±0.05 compared with 0.05±0.04, $P < 0.001$).

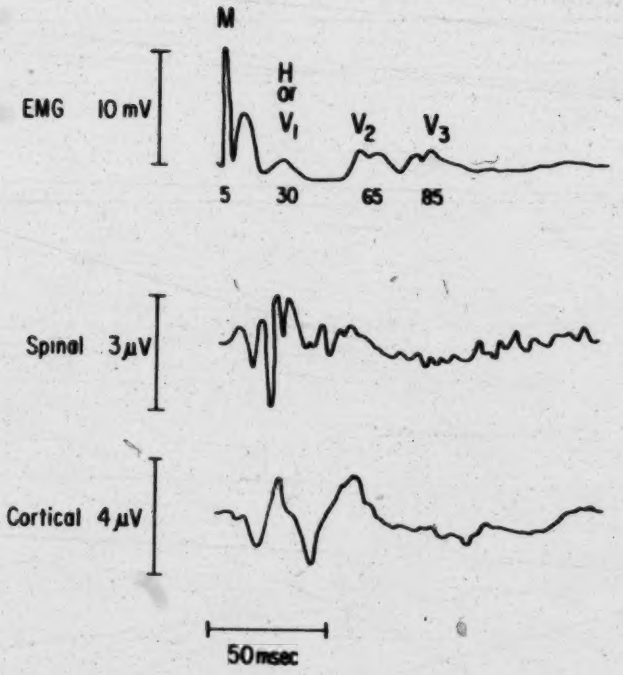

Fig. 39. Average surface EMG (after rectification), average spinal and average cortical evoked responses produced by electrical stimuli to the median nerve. The surface EMG recorded from the skin over the abductor pollicis brevis muscle showed several peaks which are discussed further in the text. The evoked responses were measured from the middle of the neck or from the scalp over the contralateral hand area of the motor cortex. An electrode on the ipsilateral ear served as an indifferent electrode for both responses. All traces are averages of 200 sweeps and the evoked responses are displayed with negative upward.

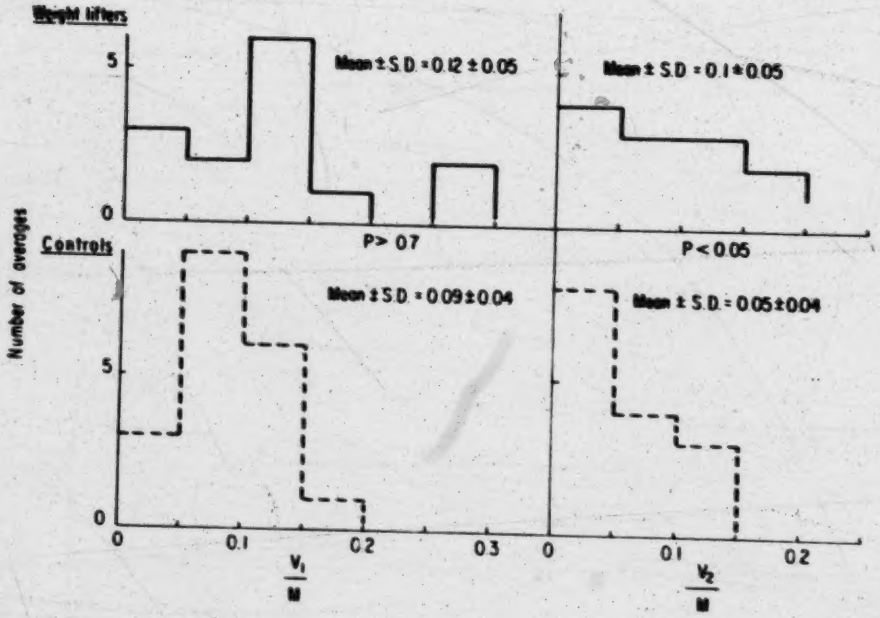

Fig. 40. Histogram of V_1 and V_2 waves relative to maximum M waves, calculated for four weightlifters and five controls. The distribution of the $\frac{V_1}{M}$ ratios were not significantly different ($P > 0.7$), but the distribution of the $\frac{V_2}{M}$ ratios were significantly different ($P < 0.001$).

One subject who regularly lifted weights showed a decrease in all three waves (especially V_2 and V_3) after laying off for two months. While lifting weights regularly this subject's mean V_1, V_2 and V_3, relative to maximum M were 0.14, 0.17 and 0.24 respectively; after laying off for two months the corresponding values decreased to 0.07, 0.04 and 0.08 respectively.

CHAPTER VII

DISCUSSION (2)

VII.1 Pattern of recruitment of motor units

The results from Section VI.1 give new quantitative data on the nature of regeneration in human motor units. Given a reasonable period of time after surgical repair of a completely severed ulnar nerve, the twitch tensions of single motor units returned to normal. Any remaining deficit in strength should be due to a reduction in the total number of motor units, due to the inability of some motor axons to reach the muscle and re-innervate muscle fibers. Gutmann and Sanders (1943) found that one year after severance and suture of the peroneal nerve of rabbits, there were fewer fibers in the periphery than in the central stump, but the pattern of fiber sizes of the nerve returned to normal. The possibility of a reduced number of motor units could be tested using recently developed methods for estimating the number of motor units in a muscle (McComas, Fawcett, Campbell & Sica, 1971). In this method incremental responses are recorded from the muscle as the stimuli to the innervating nerve are gradually increased above the threshold level. On the assumption that each increment represented the recruitment of an additional motor unit, it is possible to calculate the average size of a motor unit potential; by dividing this average value into maximum evoked muscle response an approximate estimate of the number of motor units in the muscle can be obtained.

It was intriguing to find that the normal orderly pattern of recruiting larger and larger motor units during increasing voluntary

contraction was irretrievably lost after complete severance of a nerve. It is not at all obvious why this orderly pattern appears during normal development, but does not reappear following complete severance and regeneration of the nerve. Perhaps during development larger α-motoneurons begin to sprout axons somewhat earlier and so reach more uninnervated muscle fibers than do the smaller α-motoneurons. An analogous situation would be the earlier myelination of larger axons in developing nerves.

Different types of fibers are known to reach and innervate end organs at different times during development. For example, Diamond and Miledi (1962) found miniature end-plate potentials in rat muscles five days before birth. A considerable number of spontaneous contractions were observed in most foetal diaphragms, accompanied by muscle fiber action potentials. D-tubocurarine greatly reduced or abolished the spontaneous mechanical activity, which indicates that ACh was at least partly responsible for it. Also, stimulation of the phrenic nerve in the foetuses elicited a contraction in the muscle. These results suggest the establishment of innervation by α-motoneurons in the foetal muscle fibers. Primary muscle spindle afferents also have begun to cause differentiation of intrafusal muscle fibers three days before birth in the rat (Zelená, 1964). Innervation by smaller motor and sensory fibers only occur after birth. Afferents which supply Golgi tendon organs (and which are somewhat smaller than primary muscle spindle afferents) are seen three days after birth. The γ-motoneurons can be distinguished five to ten days after birth, and the smaller secondary muscle spindle afferents also appear about this time (Zelená, 1964).

Thus, there appears to be a correlation between the size of different fiber types and their order of innervation. Whether this correlation holds within a given fiber type, a population of α-motoneurons remains to be tested. As indicated above, this hypothesis could explain the relation between the size of a motoneuron and the number of muscle fibers it innervates.

Anatomical evidence indicates that the cell body is smaller for a neuron with a small axon than for one with a large axon (Hodes, 1949). A large axon will generally innervate more muscle fibers (Henneman, 1968) and thus one associates a larger cell body with a larger motor unit. Experiments on cat lumbosacral α-motoneurons (Kernell, 1966) showed that, in comparison with large cells possessing rapidly conducting axons, the small cells with slowly conducting axons have the higher input impedance, and they need weaker stimulating currents to reach the threshold for repetitive firing. This would then account for the 'size principle'. For eliciting a steady repetitive discharge (which occurs during a brief maintained voluntary contraction), the threshold current strength is linearly related to the inverse of the input impedance. This explains the orderly recruitment of motor units.

The homogeneous character of a motor unit is the natural result of the uniform neural control exerted by the motor neuron over its muscle fibers during their period of differentiation. This control may be trophic in nature or it may be due to neural regulation of the intensity of muscular activity. In experiments on fast and slow muscles whose nerves had been transposed at an early age, Buller *et al.* (1960)

concluded that nerves exert a controlling influence over muscles at the time of their differentiation into fast and slow types. Whatever the nature of this influence may be, it is evidently powerful and precise, for it enables each motoneuron to specify the contractile properties of its muscle fibers within narrow limits. As a consequence the functional properties of each motoneuron are closely matched with those of all its muscle fibers. Although the first dorsal interosseus muscle is rather small, the range of twitch tensions (< 1g to > 20 g) and contraction times (~ 40 msec to 100 msec) recorded indicate a wide range of motor unit size, with quite a spread of threshold excitability. These inherent motor unit properties which are established during development result in an orderly recruitment of motor units according to size. Given an even start following nerve section in later life, nerve fibers of different size grow at similar rates (Gutmann *et al.*, 1942; Lubińska, 1964), and the number of types of muscle fibers innervated would be random. It is then possible that muscle fibers previously innervated by small high impedance motoneurons would be re-innervated by larger low impedance motoneurons. This randomness of re-innervation might disrupt the homogeneous character of the motor units, and probably the orderly pattern of recruitment.

In pressure or entrapment neuropathies in which the ulnar nerve is not severed there is always a physically continuous path between nerve and muscle fibers, and the normal orderly pattern for recruiting motor units was still evident. When the nerve trunk is not severed and axons are blocked without much disorganization of the myelin channels, regrowing sprouts may follow the pre-existing route across the point of

injury and down to the muscle again following surgical decompression of the nerve. This explanation could account for the orderly pattern of recruitment found in partially recovered patients, who had only one or two functional units before surgery. Similar results on the pattern of recruitment from motor neuron disease patients support the suggestion that a maintained physical continuity between nerve and muscle is a necessary condition for the preservation of the orderly recruitment of motor units during voluntary contraction.

VII.2 Contractile and electrical properties of motor units

Some quantitative data of the contractile and electrical properties of motor units, altered by neuropathies and motor neuron disease, have been presented in the study in Section VI.2. The increased EMG amplitude among patients with ulnar neuropathies and motor neuron disease are consistent with the idea that any remaining "healthy" motoneurons may sprout new collaterals to innervate muscle fibers that had been previously denervated (Erminio *et al.*, 1959; Wohlfart, 1957, 1958; Coërs & Woolf, 1959). However, these experiments do not rule out the possibility that the atrophy and reduction of total muscle mass often seen in these patients reduces the shunting of the signals produced by motor units so that the signals recorded are larger. Since this increase is observed with surface as well as with needle electrodes, the decreased shunting would have to be quite widespread.

In view of the evidence in favour of collateral sprouting presented in the studies quoted above, this represents the more plausible explanation of our increased EMG amplitudes. However, if there is an

increase in the number of muscle fibers per motor unit as a result of sprouting, the tendency for the twitch tensions to be *smaller* in ulnar neuropathies is all the more surprising. The enlarged motor unit appears to be a less efficient mechanical unit. This decreased efficiency could result from (1) a deficiency in excitation-contraction coupling; or (2) a deficiency in the coupling of the contraction to an external recording device. Using scanning electron microscopy, Sakuragawa, Sato and Tsubaki (1973) found that in the early stage of neurogenic atrophy due to peripheral neuropathy, there was a disappearance of the openings of the T tubules and a loss of the A-I banding pattern. A number of other factors could also contribute to the first category, such as (a) a decreased trophic influence of motoneurons on individual muscle fibers of the enlarged motor unit, leading for example to decreased enzymatic activity; (b) an increased susceptability to fatigue. The experiments of Edwards and Lippold (1956), indicating that the integrated EMG required to maintain a constant force increases during fatigue, suggests that a substantial decrease takes place during fatigue in the efficiency of excitation-contraction coupling. More recent evidence (Stephens & Taylor, 1970) also implicates other factors in fatigue of normal human muscle. These authors postulated that "in a maximal voluntary contraction, neuromuscular junction fatigue is most important at first (< 1 min) but later, fatigue of contractile elements increases, particularly when the blood supply is obstructed. Also neuromuscular junction fatigue was believed to be most marked in high threshold units, while fatigue of contractile elements particularly affected low threshold units". These experiments could be repeated

patients suffering from ulnar neuropathies to test whether the common clinical observation that the muscles of the affected hands tire more easily is due to a defect in excitation-contraction coupling.

The above arguments seem to contradict previous data obtained by McComas, Sica, Campbell and Upton (1971) in partially denervated muscles using stimulation techniques (Sica & McComas, 1971). In their study single twitches of the extensor digitorum brevis in patients with motor neuron disease were larger than normal. In addition, they calculated the ratio of the maximum twitch tension to that of the maximum evoked muscle response and obtained 59 g/mV for controls, while in muscles with more than 90% denervation, the value was 78 g/mV. Our results, however, indicate that during a maintained voluntary contraction, the distribution of twitch tensions averaged over a period of about 2 minutes were within the normal range in patients with motor neuron disease. Also, the corresponding ratio of mean twitch tension to mean EMG amplitude calculated from our data gives the values 21 g/mV and 4 g/mV for normals and motor neuron disease patients respectively. This discrepancy could arise from differences in the two muscles, but the data are consistent with the hypothesis that enlarged motor units may be particularly susceptible to fatigue. Thus a single stimulus could give a greater tension, as found by McComas *et al.* (1971), but with maintained use the tension might fall to within the normal range, as indicated by our results.

The second explanation suggested above, a deficiency in the coupling of the internal contraction to an external recording device, could result from fibrosis within the muscle. Fibrosis might also slow

the contraction and relaxation times as observed experimentally. A slowing of these times might also result from decreased excitation-contraction coupling (Mannard & Stein, 1973): in this study, the tension in the muscle eventually begins to decline, during maintained stimulation of the soleus nerve. This may be accompanied by an increase in damping and a decrease in natural frequency, implying that the response of a fatiguing muscle to any variation in the neural signal becomes more sluggish. It is likely that several of these factors contribute to making the enlarged motor units in neuromuscular disease more sluggish and less efficient.

VII.3 Synchronization of motor units

In the initial study of the contractile properties of normal human motor units (Chapters IV and V), only one out of the six subjects showed significant synchronization. Five of the neuropathic patients showed synchronized motor unit activity in their normal hand; however, synchronization was much less prominent or absent on the affected side. This finding of a reduced synchronization of motor units in ulnar neuropathies raised a fundamental question. Why do some individuals show synchronization while others do not? It was noted that most of the patients who showed synchronization were involved in manual jobs, which required large, brief forces to be exerted. Incidentally, the first subject who showed a high degree of synchronization regularly lifted weights. Perhaps the regular use of these muscles to exert large, brief forces leads not only to hypertrophy of the muscles involved, but also to changes in the central nervous system. These changes

result in motor units being activated nearly synchronously, even during the generation of steady forces where this synchronization is not required. To test this hypothesis, six other weightlifters were studied and all showed clear evidence of synchronization. If 20% of the population show synchronization, as Buchthal and Madsen (1950) suggested, then the chances of finding synchronization in each of seven individuals chosen at random would be less than 10^{-4}. Since all the seven subjects who lifted weights showed synchronization in most of their motor units, this provides strong evidence for the hypothesis.

How does this synchronization develop? One can imagine two types of mechanisms. Either the connections from sensory fibers to spinal motoneurons could be strengthened, or descending inputs (e.g., monosynaptic inputs from motor cortex via the pyramidal tract; Phillips, 1969) could be enhanced. Strong excitatory inputs from either source to a motoneuron pool would tend to synchronize the discharge of motoneurons, as found experimentally. Inhibitory inputs to a motoneuron pool would not be effective in producing the type of synchronization observed (Chapter V; Moore *et al.*, 1970) so this possibility will not be considered further. To distinguish between spinal reflexes and supraspinal mechanisms, reflex experiments were performed on weightlifters and non-weightlifters. The EMG record showed an early V_1 or spinal H-reflex wave, and later V_2 and V_3 waves, whose latencies suggest supraspinal and possibly cortical reflexes.

The average latency of the peaks in the cortical evoked potentials was only 24 msec (see also Cracco, 1972) which allows adequate time for a "cortical reflex" to reach the muscle by 60 msec.

Such cortical reflexes have been suggested from animal experiments (Phillips, 1969; Evarts, 1973). From his extensive electrophysiological study on the cortical control of the baboon's hand, Phillips (1969) was led to suggest that the spinal stretch reflex arc had "been overlaid in the course of evolution by a transcortical circuit". Such a transcortical reflex derives its plausibility from the finding that impulses from muscle spindle afferents have a rapid pathway to the cerebral cortex, forming the afferent limb of the loop. First found in lower animals, this pathway has been traced in the baboon to a cortical area in the depths of the central sulcus, next to the motor area (Phillips, 1971). The efferent limb of the loop is formed by the fast corticospinal (pyramidal tract) fibers, many of which in the baboon's hand (and, therefore it may be presumed in the human hand, too) end monosynaptically upon the spinal motoneurons. Evarts has also seen the transcortical reflex at work in conscious monkeys performing a trained task. When the arm in use was displaced without warning, a corrective action was apparent in the EMG of the arm muscles. The EMG showed changes of muscle activity at an initial latency of 12 msec, then a second phase of muscle activity began at a latency of 30 to 40 msec and a third phase began at about 80 msec. Initially the naive monkey did not exhibit the later EMG waves; only gradually after learning the task did the monkey acquire this EMG response. Concurrently, single pyramidal tract neurons under observation in the motor cortex altered their discharge frequency after as little as 20 to 24 msec. This was early enough for the pyramidal cells to be responsible for the corrective action at the 30 to 40 msec latency, for electrical stimulation experi-

ments showed that the conduction time for pyramidal cell to forearm muscles was only 7 msec in the fastest fibers. Evarts proposed from his findings that neurons of primate motor cortex may function in a transcortical servo~~-loop~~.

Marsden, Merton and Morton (1973) have also proposed that in the human stretch reflex proper, a transcortical pathway may be involved. Indeed, Murphy and Wong (1974) have recently described cortical activity in conscious monkeys at two latencies (11 msec and 17 msec). The first involved a fast, ascending pathway such as the medial lemniscus, while the second was blocked by cooling Dieter's nucleus and so involved the cerebellum. The finding of two later waves in man (V_2 and V_3) is suggestive of similar mechanisms, but further experiments are needed to test this possibility. In addition to the regular occurrence of a V_3 wave in the weightlifters, the wave was strongly potentiated and was on the average twice as great (relative to the maximum M) in weightlifters as in control subjects.

The V_1 or spinal reflex was also somewhat greater relative to the M-wave in weightlifters, though the difference between weightlifters and control subjects was not significant with the small sample size. The overall picture is summarized schematically in Fig. 41. Stimulation evokes a direct motor response (M wave), a spinal reflex (H or V_1 wave), and later waves which may involve the motor cortex and possible the cerebellum (V_2 and V_3 waves). The later supraspinal waves are particularly prominent in weightlifters and so may be potentiated by regular, brief, near-maximal contractions of a muscle. These preliminary results suggest for the first time specific neuronal pathways which are enhanced

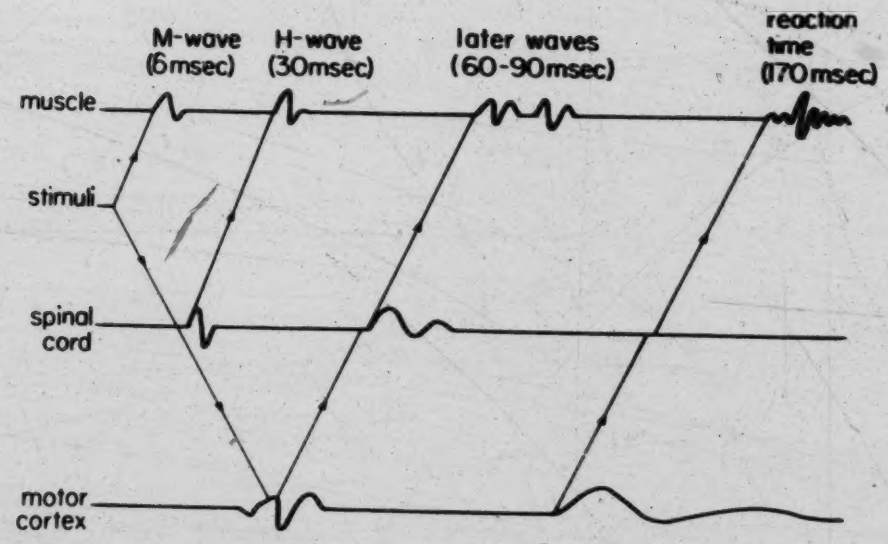

Fig. 41. Idealized representation of the responses to median nerve stimulation. Direct motor (M) waves, spinal reflex (H or V_1) waves and later supraspinal reflex (V_2 and V_3) waves are observed, which all occur much earlier than the normal reaction time to an electrical stimulus.

by a specific form of physical training. It can also be deduced from these results that the main changes in the motoneuron pool, resulting from weightlifting, which affect these reflexes, are not due to afferents from muscle spindles, but due to descending inputs from higher centers. If these reflex results are applied to voluntary contractions, then there is an indication that the changes in the motoneuron pool, which result in synchronization, are due mainly to the influence of descending supraspinal pathways. The efficiency of these descending pathways may be increased by regular use, resulting in an increase in synchronization and decreased by disuse. Further work will be carried out in the near future to further test this idea.

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